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LOGINID:ssspta1604dxj

PASSWORD:
TERMINAL (ENTER 1, 2, 3, OR ?):2

* * * * * * * * * * Welcome to STN International * * * * * * * * * *

NEWS 1		Web Page for STN Seminar Schedule - N. America
NEWS 2	OCT 02	CA/CAplus enhanced with pre-1907 records from Chemisches Zentralblatt
NEWS 3	OCT 19	BEILSTEIN updated with new compounds
NEWS 4	NOV 15	Derwent Indian patent publication number format enhanced
NEWS 5	NOV 19	WPIX enhanced with XML display format
NEWS 6	NOV 30	ICSD reloaded with enhancements
NEWS 7	DEC 04	LINPADOCDB now available on STN
NEWS 8	DEC 14	BEILSTEIN pricing structure to change
NEWS 9	DEC 17	USPATOLD added to additional database clusters
NEWS 10	DEC 17	IMSDRUGCONF removed from database clusters and STN
NEWS 11	DEC 17	DGENE now includes more than 10 million sequences
NEWS 12	DEC 17	TOXCENTER enhanced with 2008 MeSH vocabulary in MEDLINE segment
NEWS 13	DEC 17	MEDLINE and LMEDLINE updated with 2008 MeSH vocabulary
NEWS 14	DEC 17	CA/CAplus enhanced with new custom IPC display formats
NEWS 15	DEC 17	STN Viewer enhanced with full-text patent content from USPATOLD
NEWS 16	JAN 02	STN pricing information for 2008 now available
NEWS 17	JAN 16	CAS patent coverage enhanced to include exemplified prophetic substances
NEWS 18	JAN 28	USPATFULL, USPAT2, and USPATOLD enhanced with new custom IPC display formats
NEWS 19	JAN 28	MARPAT searching enhanced
NEWS 20	JAN 28	USGENE now provides USPTO sequence data within 3 days of publication
NEWS 21	JAN 28	TOXCENTER enhanced with reloaded MEDLINE segment
NEWS 22	JAN 28	MEDLINE and LMEDLINE reloaded with enhancements
NEWS 23	FEB 08	STN Express, Version 8.3, now available
NEWS 24	FEB 20	PCI now available as a replacement to DPCI
NEWS 25	FEB 25	IFIREF reloaded with enhancements
NEWS 26	FEB 25	IMSPRODUCT reloaded with enhancements
NEWS 27	FEB 29	WPINDEX/WPIDS/WPIX enhanced with ECLA and current U.S. National Patent Classification

NEWS EXPRESS FEBRUARY 08 CURRENT WINDOWS VERSION IS V8.3,
AND CURRENT DISCOVER FILE IS DATED 20 FEBRUARY 2008

NEWS HOURS STN Operating Hours Plus Help Desk Availability
NEWS LOGIN Welcome Banner and News Items

Jagoe

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 NEWS IPC8     For general information regarding STN implementation of IPC 8

Enter NEWS followed by the item number or name to see news on that
specific topic.

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* * * * * * * * * * * * * * * * STN  Columbus  * * * * * * * * * * * * * * * *

FILE 'HOME' ENTERED AT 08:55:09 ON 03 MAR 2008

=> file reg
COST IN U.S. DOLLARS                                SINCE FILE      TOTAL
                                                         ENTRY    SESSION
FULL ESTIMATED COST                                       0.21       0.21

FILE 'REGISTRY' ENTERED AT 08:55:39 ON 03 MAR 2008
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Property values tagged with IC are from the ZIC/VINITI data file
provided by InfoChem.

STRUCTURE FILE UPDATES:    2 MAR 2008  HIGHEST RN 1006303-40-7
DICTIONARY FILE UPDATES:   2 MAR 2008  HIGHEST RN 1006303-40-7

New CAS Information Use Policies, enter HELP USAGETERMS for details.

TSCA INFORMATION NOW CURRENT THROUGH January 9, 2008.

  Please note that search-term pricing does apply when
  conducting SmartSELECT searches.

REGISTRY includes numerically searchable data for experimental and
predicted properties as well as tags indicating availability of
experimental property data in the original document.  For information
on property searching in REGISTRY, refer to:

http://www.cas.org/support/stngen/stndoc/properties.html

=> s montlukast/cn
L1            0 MONTLUKAST/CN

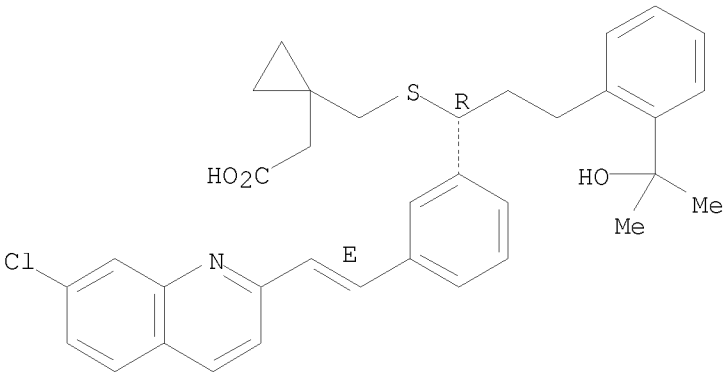
=> s montelukast/cn
L2            1 MONTELUKAST/CN

=> d l2

L2   ANSWER 1 OF 1  REGISTRY  COPYRIGHT 2008 ACS on STN
RN   158966-92-8  REGISTRY
ED   Entered STN:  15 Nov 1994
```

CN Cyclopropaneacetic acid, 1-[[[(1R)-1-[3-[(1E)-2-(7-chloro-2-quinolinyl)ethenyl]phenyl]-3-[2-(1-hydroxy-1-methylethyl)phenyl]propyl]thio]methyl]- (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN Cyclopropaneacetic acid, 1-[[[1-[3-[2-(7-chloro-2-quinolinyl)ethenyl]phenyl]-3-[2-(1-hydroxy-1-methylethyl)phenyl]propyl]thio]methyl]-, [R-(E)]-
OTHER NAMES:
CN 1-[[[(R)-1-[3-[(E)-2-(7-Chloro-2-quinolinyl)ethenyl]phenyl]-3-[2-(1-hydroxy-1-methylethyl)phenyl]propyl]thio]methyl]cyclopropaneacetic acid
CN 2-[1-[[[(1R)-1-[3-[(1E)-2-(7-Chloro-2-quinolinyl)ethenyl]phenyl]-3-[2-(1-hydroxy-1-methylethyl)phenyl]propyl]thio]methyl]cyclopropyl]acetic acid
CN Montelukast
FS STEREOSEARCH
MF C35 H36 Cl N O3 S
CI COM
SR World Health Organization (WHO)
LC STN Files: ADISINSIGHT, ADISNEWS, AGRICOLA, BIOSIS, BIOTECHNO, CA, CAPLUS, CASREACT, CHEMCATS, CIN, DDFU, DRUGU, EMBASE, IMSCOSEARCH, IMSDRUGNEWS, IMSPATENTS, IMSPRODUCT, IMSRESEARCH, IPA, MEDLINE, MRCK*, PATDPASPC, PROMT, PROUSDDR, PS, RTECS*, SYNTHLINE, TOXCENTER, USAN, USPAT2, USPATFULL
(*File contains numerically searchable property data)
Other Sources: WHO

Absolute stereochemistry.
Double bond geometry as shown.



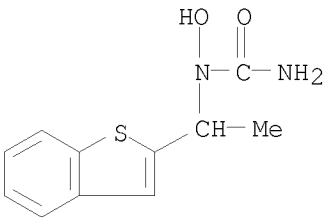
PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

595 REFERENCES IN FILE CA (1907 TO DATE)
17 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
603 REFERENCES IN FILE CAPLUS (1907 TO DATE)

=> s zileuton/cn
L3 1 ZILEUTON/CN

=> d l3

L3 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2008 ACS on STN
RN 111406-87-2 REGISTRY
ED Entered STN: 21 Nov 1987
CN Urea, N-(1-benzo[b]thien-2-ylethyl)-N-hydroxy- (CA INDEX NAME)
OTHER NAMES:
CN A 64077
CN Abbott 64077
CN Leutrol
CN N-(1-Benzo[b]thien-2-ylethyl)-N-hydroxyurea
CN Zileuton
CN Zyflo
DR 133305-01-8, 154003-29-9
MF C11 H12 N2 O2 S
CI COM
SR US Adopted Names Council (USAN)
LC STN Files: ADISINSIGHT, ADISNEWS, AGRICOLA, ANABSTR, BEILSTEIN*, BIOSIS, BIOTECHNO, CA, CAPLUS, CASREACT, CBNB, CHEMCATS, CHEMINFORMRX, CHEMLIST, CIN, CSCHEM, DDFU, DRUGU, EMBASE, IMSDRUGNEWS, IMSPATENTS, IMSPRODUCT, IMSRESEARCH, IPA, MRCK*, PHAR, PROMT, PROUSDDR, PS, RTECS*, SYNTHLINE, TOXCENTER, USAN, USPAT2, USPATFULL
(*File contains numerically searchable property data)



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

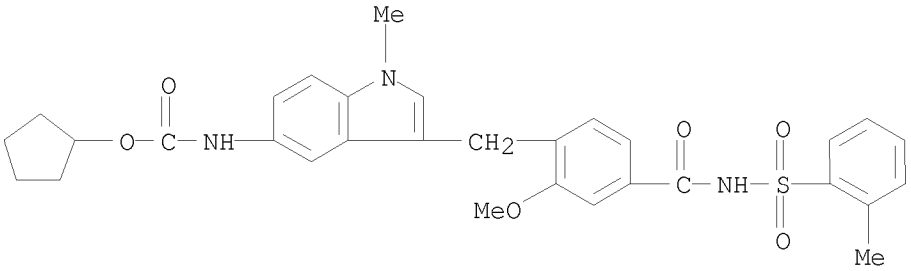
396 REFERENCES IN FILE CA (1907 TO DATE)
5 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
396 REFERENCES IN FILE CAPLUS (1907 TO DATE)

=> s zafirlukast/cn
L4 1 ZAFIRLUKAST/CN

=> d l4

L4 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2008 ACS on STN
RN 107753-78-6 REGISTRY
ED Entered STN: 26 Apr 1987
CN Carbamic acid, N-[3-[[2-methoxy-4-[[[(2-methylphenyl)sulfonyl]amino]carbonyl]phenyl]methyl]-1-methyl-1H-indol-5-yl]-, cyclopentyl ester (CA INDEX NAME)

OTHER CA INDEX NAMES:
CN Carbamic acid, [3-[[2-methoxy-4-[[[(2-methylphenyl)sulfonyl]amino]carbonyl]phenyl]methyl]-1-methyl-1H-indol-5-yl]-, cyclopentyl ester (9CI)
OTHER NAMES:
CN Accolate
CN Cyclopentyl 3-[2-methoxy-4-[(o-tolylsulfonyl)carbamoyl]benzyl]-1-methylindole-5-carbamate
CN ICI 204219
CN Vanticon
CN Zafirlukast
MF C31 H33 N3 O6 S
CI COM
SR CA
LC STN Files: ADISINSIGHT, ADISNEWS, AGRICOLA, ANABSTR, BEILSTEIN*, BIOSIS, BIOTECHNO, CA, CAPLUS, CASREACT, CBNB, CHEMCATS, CIN, CSCHEM, DDFU, DRUGU, EMBASE, IMSDRUGNEWS, IMSPATENTS, IMSPRODUCT, IMSRESEARCH, IPA, MEDLINE, MRCK*, PHAR, PROMT, PROUSDDR, PS, RTECS*, SYNTHLINE, TOXCENTER, USAN, USPAT2, USPATFULL
(*File contains numerically searchable property data)
Other Sources: WHO



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

390 REFERENCES IN FILE CA (1907 TO DATE)
9 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
391 REFERENCES IN FILE CAPLUS (1907 TO DATE)

=> s ?lukast
LEFT TRUNCATION IGNORED FOR FILE 'REGISTRY'
L5 4 LUKAST
Left truncation is not valid in the specified search field in the specified file. The term has been searched without left truncation. Examples: '?TERPEN?' would be searched as 'TERPEN?' and '?FLAVONOID' would be searched as 'FLAVONOID.'

If you are searching in a field that uses implied proximity, and you used a truncation symbol after a punctuation mark, the system may interpret the truncation symbol as being at the beginning of a term.

Implied proximity is used in search fields indexed as single words,
for example, the Basic Index.

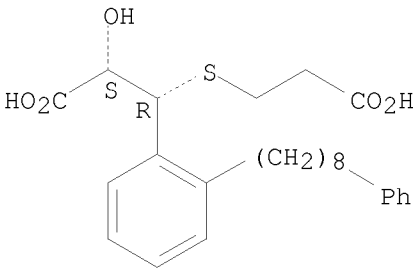
=> d l5 1-4

L5 ANSWER 1 OF 4 REGISTRY COPYRIGHT 2008 ACS on STN
RN 385390-37-4 REGISTRY
ED Entered STN: 22 Jan 2002
CN Benzenepropanoic acid, β-[(2-carboxyethyl)thio]-α-hydroxy-2-(8-phenyloctyl)-, (αS,βR)-, compd. with 1,2-ethanediamine (1:1) (9CI) (CA INDEX NAME)
OTHER NAMES:
CN Pobilukast edamine
FS STEREOSEARCH
MF C26 H34 O5 S . C2 H8 N2
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER, USPAT2, USPATFULL

CM 1

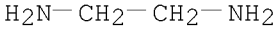
CRN 107023-41-6
CMF C26 H34 O5 S

Absolute stereochemistry. Rotation (-).



CM 2

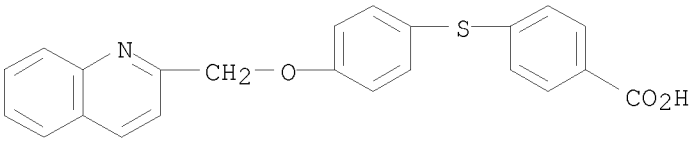
CRN 107-15-3
CMF C2 H8 N2



3 REFERENCES IN FILE CA (1907 TO DATE)
3 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L5 ANSWER 2 OF 4 REGISTRY COPYRIGHT 2008 ACS on STN
RN 252972-08-0 REGISTRY
ED Entered STN: 18 Jan 2000
CN Benzoic acid, 4-[[4-(2-quinolinylmethoxy)phenyl]thio]- (CA INDEX NAME)

OTHER NAMES:
CN Quinlukast
CN VUFB 19363
MF C23 H17 N O3 S
CI COM
SR CA
LC STN Files: ADISINSIGHT, ANABSTR, CA, CAPLUS, CASREACT, CHEMCATS, PROUSDDR, SYNTHLINE, TOXCENTER, USPATFULL



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

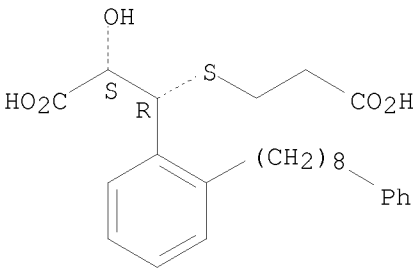
13 REFERENCES IN FILE CA (1907 TO DATE)
13 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L5 ANSWER 3 OF 4 REGISTRY COPYRIGHT 2008 ACS on STN
RN 137232-03-2 REGISTRY
ED Entered STN: 08 Nov 1991
CN Benzenepropanoic acid, β-[(2-carboxyethyl)thio]-α-hydroxy-2-(8-phenyloctyl)-, [R-(R*,S*)]-, compd. with 1,2-ethanediamine (1:1), monohydrate (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN 1,2-Ethanediamine, mono[[R-(R*,S*)]-β-[(2-carboxyethyl)thio]-α-hydroxy-2-(8-phenyloctyl)benzenepropanoate], monohydrate (9CI)
OTHER NAMES:
CN (2S,3R)-3-[(2-Carboxyethyl)thio]-3-[o-(8-phenyloctyl)phenyl]lactic acid, compound with ethylenediamine (1:1), monohydrate
CN Pobilukast edamine hydrate
FS STEREOSEARCH
MF C26 H34 O5 S . C2 H8 N2 . H2 O
SR US Adopted Names Council (USAN)
LC STN Files: ADISINSIGHT, IMSPATENTS, IMSRESEARCH, PROUSDDR, SYNTHLINE, USAN
Other Sources: WHO

CM 1

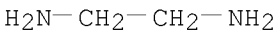
CRN 107023-41-6
CMF C26 H34 O5 S

Absolute stereochemistry. Rotation (-).



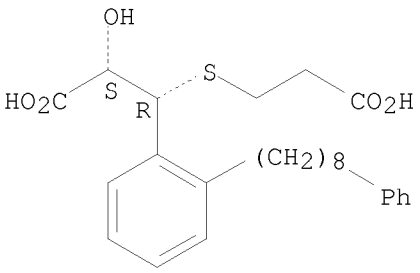
CM 2

CRN 107-15-3
CMF C2 H8 N2



L5 ANSWER 4 OF 4 REGISTRY COPYRIGHT 2008 ACS on STN
RN 107023-41-6 REGISTRY
ED Entered STN: 14 Mar 1987
CN Benzenepropanoic acid, β-[(2-carboxyethyl)thio]-α-hydroxy-2-(8-phenyloctyl)-, (αS,βR)- (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN Benzenepropanoic acid, β-[(2-carboxyethyl)thio]-α-hydroxy-2-(8-phenyloctyl)-, [R-(R*,S*)]-
OTHER NAMES:
CN Pobilukast
CN SKF 104353
FS STEREOSEARCH
DR 108116-14-9
MF C26 H34 O5 S
CI COM
SR CA
LC STN Files: ADISINSIGHT, ADISNEWS, BEILSTEIN*, BIOSIS, BIOTECHNO, CA, CAPLUS, CASREACT, DDFU, DRUGU, EMBASE, IMSDRUGNEWS, IMSPATENTS, IMSRESEARCH, IPA, MEDLINE, PHAR, PROUSDDR, SYNTHLINE, TOXCENTER, USAN, USPAT2, USPATFULL
(*File contains numerically searchable property data)

Absolute stereochemistry. Rotation (-).



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

52 REFERENCES IN FILE CA (1907 TO DATE)
52 REFERENCES IN FILE CAPLUS (1907 TO DATE)

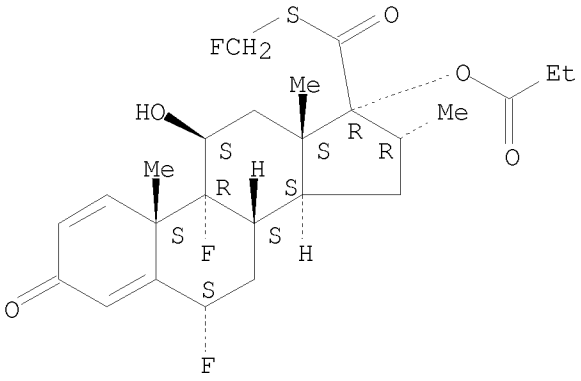
=> s fluticasone propionate/cn
L6 1 FLUTICASONE PROPIONATE/CN

=> d l6

L6 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2008 ACS on STN
RN 80474-14-2 REGISTRY
ED Entered STN: 16 Nov 1984
CN Androsta-1,4-diene-17-carbothioic acid, 6,9-difluoro-11-hydroxy-16-methyl-3-oxo-17-(1-oxopropoxy)-, S-(fluoromethyl) ester, (6α,11β,16α,17α)- (CA INDEX NAME)
OTHER NAMES:
CN Atemur Mite
CN CCI 18781
CN Cutivate
CN Cutivate cream
CN Cyclesonide
CN Flixonase
CN Flixonase Nasal Spray
CN Flixotide
CN Flixotide Disk
CN Flixotide Disks
CN Flixotide Inhaler
CN Flonase
CN Flonase Aq
CN Flovent
CN Flovent Diskus
CN Flunase
CN Fluticasone 17-propionate
CN Fluticasone propionate
CN Flutide
CN Flutide N
CN Flutivate
CN Zoflut
FS STEREOSEARCH
MF C25 H31 F3 O5 S

CI COM
LC STN Files: ADISINSIGHT, ADISNEWS, AGRICOLA, ANABSTR, BIOSIS, BIOTECHNO, CA, CAPLUS, CASREACT, CBNB, CHEMCATS, CHEMLIST, CIN, CSCHEM, DDFU, DRUGU, EMBASE, IMSCOSEARCH, IMSDRUGNEWS, IMSPATENTS, IMSPRODUCT, IMSRESEARCH, IPA, MEDLINE, MRCK*, MSDS-OHS, PATDPASPC, PHAR, PIRA, PROMT, PROUSDDR, PS, RTECS*, SCISEARCH, SYNTHLINE, TOXCENTER, USAN, USPAT2, USPATFULL
(*File contains numerically searchable property data)

Absolute stereochemistry.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1154 REFERENCES IN FILE CA (1907 TO DATE)
6 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
1162 REFERENCES IN FILE CAPLUS (1907 TO DATE)

=> s mometasone fuorate monohydrate/cn
L7 0 MOMETASONE FUORATE MONOHYDRATE/CN

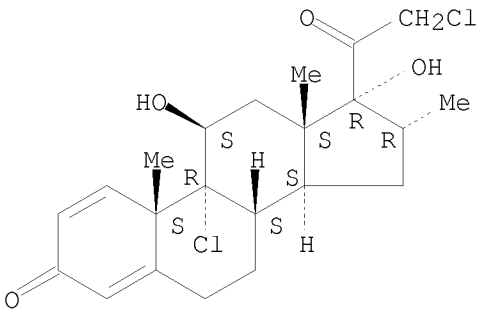
=> s mometasone/cn
L8 1 MOMETASONE/CN

=> d l8

L8 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2008 ACS on STN
RN 105102-22-5 REGISTRY
ED Entered STN: 08 Nov 1986
CN Pregna-1,4-diene-3,20-dione, 9,21-dichloro-11,17-dihydroxy-16-methyl-, (11β,16α)- (CA INDEX NAME)
OTHER NAMES:
CN (+)-Mometasone
CN Mometasone
FS STEREOSEARCH
MF C22 H28 Cl2 O4
CI COM
SR World Health Organization (WHO)
LC STN Files: ADISINSIGHT, ADISNEWS, ANABSTR, BEILSTEIN*, BIOSIS, CA,

CAPLUS, CASREACT, CBNB, CHEMCATS, CHEMLIST, CIN, IMSPATENTS,
IMSRESEARCH, PHAR, PROMT, PS, TOXCENTER, USPAT2, USPATFULL
(*File contains numerically searchable property data)
Other Sources: WHO

Absolute stereochemistry. Rotation (+).



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

291 REFERENCES IN FILE CA (1907 TO DATE)
5 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
291 REFERENCES IN FILE CAPLUS (1907 TO DATE)

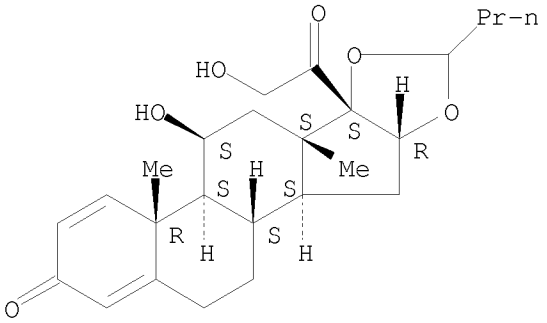
=> s budesonide/cn
L9 1 BUDESONIDE/CN

=> d l9

L9 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2008 ACS on STN
RN 51333-22-3 REGISTRY
ED Entered STN: 16 Nov 1984
CN Pregna-1,4-diene-3,20-dione, 16,17-[butylidenebis(oxy)]-11,21-dihydroxy-, (11β,16α)- (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN 2H-Naphth[2',1':4,5]indeno[1,2-d][1,3]dioxole, pregna-1,4-diene-3,20-dione deriv.
OTHER NAMES:
CN 16α,17α-(Butylidenedioxy)-11β,21-dihydroxypregna-1,4-diene-3,20-dione
CN Bidien
CN Budenofalk
CN Budeson
CN Budesonide
CN Cortivent
CN Entocort
CN Micronyl
CN Nebuampul
CN Preferid

CN Pulmicort
CN Respules
CN Rhinocort
CN Rhinocort Aqua
CN S 1320
CN Spirocort
CN Turbuhaler
FS STEREOSEARCH
MF C25 H34 O6
CI COM
LC STN Files: ADISINSIGHT, ADISNEWS, AGRICOLA, ANABSTR, BEILSTEIN*, BIOSIS, BIOTECHNO, CA, CAPLUS, CASREACT, CBNB, CHEMCATS, CHEMLIST, CIN, CSCHEM, CSNB, DDFU, DRUGU, EMBASE, IFICDB, IFIPAT, IFIUDB, IMSCOSEARCH, IMSDRUGNEWS, IMSPATENTS, IMSPRODUCT, IMSRESEARCH, IPA, MEDLINE, MRCK*, PATDPASPC, PHAR, PROMT, PROUSDDR, PS, RTECS*, SCISEARCH, SPECINFO, SYNTHLINE, TOXCENTER, USAN, USPAT2, USPATFULL
(*File contains numerically searchable property data)
Other Sources: EINECS**, WHO
(**Enter CHEMLIST File for up-to-date regulatory information)

Absolute stereochemistry.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

2201 REFERENCES IN FILE CA (1907 TO DATE)
30 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
2215 REFERENCES IN FILE CAPLUS (1907 TO DATE)

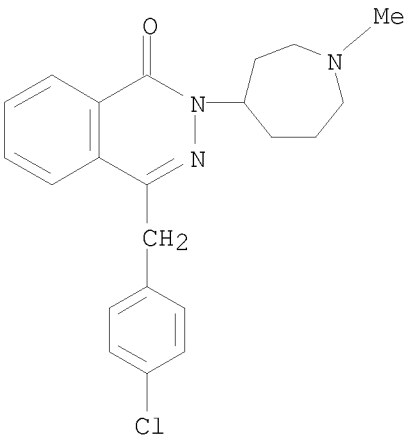
=> s azelastine/cn
L10 1 AZELASTINE/CN

=> d l10

L10 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2008 ACS on STN
RN 58581-89-8 REGISTRY
ED Entered STN: 16 Nov 1984
CN 1(2H)-Phthalazinone, 4-[(4-chlorophenyl)methyl]-2-(hexahydro-1-methyl-1H-azepin-4-yl)- (CA INDEX NAME)
OTHER NAMES:
CN (±)-Azelastine

Jagoe

CN Azelastine
DR 153483-42-2
MF C22 H24 Cl N3 O
CI COM
LC STN Files: ADISINSIGHT, ADISNEWS, AGRICOLA, ANABSTR, BEILSTEIN*, BIOSIS, BIOTECHNO, CA, CAPLUS, CASREACT, CBNB, CHEMCATS, CIN, CSCHEM, DDFU, DRUGU, EMBASE, IMSDRUGNEWS, IMSPATENTS, IMSPRODUCT, IMSRESEARCH, IPA, MEDLINE, MRCK*, PATDPASPC, PHAR, PROMT, PROUSDDR, PS, RTECS*, SCISEARCH, SYNTHLINE, TOXCENTER, USAN, USPAT2, USPATFULL
(*File contains numerically searchable property data)
Other Sources: WHO



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

523 REFERENCES IN FILE CA (1907 TO DATE)
10 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
525 REFERENCES IN FILE CAPLUS (1907 TO DATE)

=> s cetirizine/cn
L11 1 CETIRIZINE/CN

=> s fexofenadine
L12 6 FEXOFENADINE

=> s loratadine
L13 2 LORATADINE

=> s desloratadine
L14 2 DESLORATADINE

=> file medicine
FILE 'DRUGMONOG' ACCESS NOT AUTHORIZED
COST IN U.S. DOLLARS SINCE FILE TOTAL

	ENTRY	SESSION
FULL ESTIMATED COST	101.92	102.13

FILE 'ADISCTI' ENTERED AT 09:06:08 ON 03 MAR 2008

FILE 'ADISINSIGHT' ENTERED AT 09:06:08 ON 03 MAR 2008

FILE 'ADISNEWS' ENTERED AT 09:06:08 ON 03 MAR 2008

FILE 'BIOSIS' ENTERED AT 09:06:08 ON 03 MAR 2008

FILE 'BIOTECHNO' ENTERED AT 09:06:08 ON 03 MAR 2008

FILE 'CAPLUS' ENTERED AT 09:06:08 ON 03 MAR 2008

FILE 'DDFB' ENTERED AT 09:06:08 ON 03 MAR 2008

FILE 'DDFU' ACCESS NOT AUTHORIZED

FILE 'DGENE' ENTERED AT 09:06:08 ON 03 MAR 2008

FILE 'DISSABS' ENTERED AT 09:06:08 ON 03 MAR 2008

FILE 'DRUGB' ENTERED AT 09:06:08 ON 03 MAR 2008

FILE 'DRUGMONOG2' ENTERED AT 09:06:08 ON 03 MAR 2008

FILE 'DRUGU' ENTERED AT 09:06:08 ON 03 MAR 2008

FILE 'EMBAL' ENTERED AT 09:06:08 ON 03 MAR 2008

FILE 'EMBASE' ENTERED AT 09:06:08 ON 03 MAR 2008

FILE 'ESBIOBASE' ENTERED AT 09:06:08 ON 03 MAR 2008

FILE 'IFIPAT' ENTERED AT 09:06:08 ON 03 MAR 2008

FILE 'IMSDRUGNEWS' ENTERED AT 09:06:08 ON 03 MAR 2008

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FILE 'USPATOLD' ENTERED AT 09:06:08 ON 03 MAR 2008
CA INDEXING COPYRIGHT (C) 2008 AMERICAN CHEMICAL SOCIETY (ACS)

FILE 'USPAT2' ENTERED AT 09:06:08 ON 03 MAR 2008
CA INDEXING COPYRIGHT (C) 2008 AMERICAN CHEMICAL SOCIETY (ACS)

=> d his

     (FILE 'HOME' ENTERED AT 08:55:09 ON 03 MAR 2008)

     FILE 'REGISTRY' ENTERED AT 08:55:39 ON 03 MAR 2008
L1             0 S MONTLUKAST/CN
L2             1 S MONTELUKAST/CN
L3             1 S ZILEUTON/CN
L4             1 S ZAFIRLUKAST/CN
L5             4 S ?LUKAST
L6             1 S FLUTICASONE PROPIONATE/CN
L7             0 S MOMETASONE FUORATE MONOHYDRATE/CN
L8             1 S MOMETASONE/CN
L9             1 S BUDESONIDE/CN
L10            1 S AZELASTINE/CN
L11            1 S CETIRIZINE/CN
L12            6 S FEXOFENADINE
L13            2 S LORATADINE
L14            2 S DESLORATADINE

     FILE 'ADISCTI, ADISINSIGHT, ADISNEWS, BIOSIS, BIOTECHNO, CAPLUS, DDFB,
     DGENE, DISSABS, DRUGB, DRUGMONOG2, DRUGU, EMBAL, EMBASE, ESBIOBASE,
     IFIPAT, IMSDRUGNEWS, IMSPRODUCT, IPA, KOSMET, LIFESCI, MEDLINE,
     NAPRALERT, NLDB, NUTRACEUT, PASCAL, PCTGEN, PHARMAML, ...' ENTERED AT
     09:06:08 ON 03 MAR 2008

=> s l2 or l3 or l4 or l5
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L15      11824 L2 OR L3 OR L4 OR L5

=> s l6 or l8 or l9
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L16      32489 L6 OR L8 OR L9

=> s l10 or l11 or l12 or l13 or l14
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  14 FILES SEARCHED...
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'CN' IS NOT A VALID FIELD CODE
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  32 FILES SEARCHED...
'CN' IS NOT A VALID FIELD CODE
L17      32316 L10 OR L11 OR L12 OR L13 OR L14

=> s c reactive protein or inflammation
   8 FILES SEARCHED...
  33 FILES SEARCHED...
L18    2287254 C REACTIVE PROTEIN OR INFLAMMATION

=> s l15 and l16 and l17

L19        420 L15 AND L16 AND L17

=> s l18 and l19
L20        128 L18 AND L19

=> dup rem
ENTER L# LIST OR (END):120
DUPLICATE IS NOT AVAILABLE IN 'ADISINSIGHT, ADISNEWS, DGENE, DRUGMONOG2,
IMSPRODUCT, KOSMET, NUTRACEUT, PCTGEN, PHARMAML, USGENE'.
ANSWERS FROM THESE FILES WILL BE CONSIDERED UNIQUE
PROCESSING COMPLETED FOR L20
L21         100 DUP REM L20 (28 DUPLICATES REMOVED)

=> d l21 91-100 ibib, kwic

L21  ANSWER 91 OF 100  EMBASE  COPYRIGHT (c) 2008 Elsevier B.V. All rights
     reserved on STN
```

ACCESSION NUMBER: 2001368401 EMBASE <<LOGINID::20080303>>
TITLE: Effects of topical corticosteroid and combined mediator blockade on domiciliary and laboratory measurements of nasal function in seasonal allergic rhinitis.
AUTHOR: Wilson A.M.; Sims E.J.; Orr L.C.; Coutie W.J.R.; White P.S.; Gardiner Q.; Lipworth B.J.
CORPORATE SOURCE: Dr. B.J. Lipworth, Asthma and Allergy Research Group, Department of Clinical Pharmacology, Ninewells Hospital, Dundee DDI 9SY, United Kingdom. b.j.lipworth@dundee.ac.uk
SOURCE: Annals of Allergy, Asthma and Immunology, (2001) Vol. 87, No. 4, pp. 344-349.
Refs: 36
ISSN: 1081-1206 CODEN: ALAIF6
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 011 Otorhinolaryngology
015 Chest Diseases, Thoracic Surgery and Tuberculosis
026 Immunology, Serology and Transplantation
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 2 Nov 2001
Last Updated on STN: 2 Nov 2001
CT Medical Descriptors:
adult
*allergic rhinitis: DT, drug therapy
article
asthma: DT, drug therapy
clinical article
clinical trial
controlled study
crossover procedure
drug effect
female
home care
human
inflammation
laboratory test
male
*mediator release
nose airway resistance
pollen allergy
priority journal
randomized controlled trial
respiratory airflow
rhinomanometry
rhinometry
seasonal variation
single blind procedure
symptomatology
*budesonide: CT, clinical trial
*budesonide: CB, drug combination
*budesonide: DO,. . .
RN (budesonide) 51333-22-3; (cetirizine) 83881-51-0, 83881-52-1; (montelukast) 151767-02-1, 158966-92-8

L21 ANSWER 92 OF 100 EMBASE COPYRIGHT (c) 2008 Elsevier B.V. All rights reserved on STN

ACCESSION NUMBER: 2001071359 EMBASE <<LOGINID::20080303>>

TITLE: Effects of monotherapy with intra-nasal corticosteroid or combined oral histamine and leukotriene receptor antagonists in seasonal allergic rhinitis.

AUTHOR: Wilson A.M.; Orr L.C.; Sims E.J.; Lipworth B.J.

CORPORATE SOURCE: B.J. Lipworth, Asthma/Allergy Research Group, Dept. Clin. Pharmacol./Therapeut., Ninewells Hosp./Medical School, Dundee DD1 9SY, United Kingdom

SOURCE: Clinical and Experimental Allergy, (2001) Vol. 31, No. 1, pp. 61-68.
Refs: 31
ISSN: 0954-7894 CODEN: CLEAEN

COUNTRY: United Kingdom

DOCUMENT TYPE: Journal; Article

FILE SEGMENT: 011 Otorhinolaryngology
026 Immunology, Serology and Transplantation
037 Drug Literature Index
039 Pharmacy

LANGUAGE: English

SUMMARY LANGUAGE: English

ENTRY DATE: Entered STN: 16 Mar 2001
Last Updated on STN: 16 Mar 2001

CT Medical Descriptors:
adult
*allergic rhinitis: DT, drug therapy
article
clinical article
clinical trial
controlled study
crossover procedure
drug efficacy
eosinophil
human
human experiment
hydrocortisone urine level
inflammation
monotherapy
nose airflow
pollen
priority journal
randomized controlled trial
rhinomanometry
rhinometry
single blind procedure
treatment outcome
*antihistaminic agent: CT, clinical trial
*antihistaminic agent: AD, drug administration
*antihistaminic agent: CB, drug combination
*antihistaminic. . .

RN (beclometasone dipropionate) 5534-09-8; (budesonide) 51333-22-3; (cetirizine) 83881-51-0, 83881-52-1; (chlorpheniramine) 132-22-9; (loratadine) 79794-75-5; (mometasone furoate) 83919-23-7; (montelukast) 151767-02-1, 158966-92-8; (nitric oxide) 10102-43-9; (terfenadine) 50679-08-8; (triamcinolone) 124-94-7;

(zafirlukast) 107753-78-6

L21 ANSWER 93 OF 100 MEDLINE on STN DUPLICATE 25
ACCESSION NUMBER: 2001025999 MEDLINE <<LOGINID::20080303>>
DOCUMENT NUMBER: PubMed ID: 11029334
TITLE: Antiasthmatic effects of mediator blockade versus topical corticosteroids in allergic rhinitis and asthma.
AUTHOR: Wilson A M; Orr L C; Sims E J; Dempsey O J; Lipworth B J
CORPORATE SOURCE: Asthma and Allergy Research Group, Department of Clinical Pharmacology and Therapeutics, Ninewells Hospital and Medical School, University of Dundee, Dundee, Scotland, United Kingdom.
SOURCE: American journal of respiratory and critical care medicine, (2000 Oct) Vol. 162, No. 4 Pt 1, pp. 1297-301. Journal code: 9421642. ISSN: 1073-449X.
PUB. COUNTRY: United States
DOCUMENT TYPE: (CLINICAL TRIAL)
(COMPARATIVE STUDY)
Journal; Article; (JOURNAL ARTICLE)
(RANDOMIZED CONTROLLED TRIAL)
(RESEARCH SUPPORT, NON-U.S. GOV'T)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 200011
ENTRY DATE: Entered STN: 22 Mar 2001
Last Updated on STN: 22 Mar 2001
Entered Medline: 15 Nov 2000
CT . . . & dosage
Cetirizine: AE, adverse effects
Cross-Over Studies
Double-Blind Method
Drug Therapy, Combination
Forced Expiratory Volume: DE, drug effects
Humans
*Inflammation Mediators: AI, antagonists & inhibitors
*Leukotriene Antagonists: AD, administration & dosage
Leukotriene Antagonists: AE, adverse effects
*Quinolines: AD, administration &. . .
RN 158966-92-8 (montelukast); 51333-22-3 (Budesonide); 83881-51-0 (Cetirizine)
CN 0 (Acetates); 0 (Anti-Asthmatic Agents); 0 (Inflammation Mediators); 0 (Leukotriene Antagonists); 0 (Quinolines)

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ACCESSION NUMBER: 2000350797 EMBASE <<LOGINID::20080303>>
TITLE: Allergic inflammation in the unified airway: Start with the nose.
AUTHOR: Lipworth B.J.; White P.S.
CORPORATE SOURCE: Prof. B.J. Lipworth, Asthma and Allergy Research Group, Dept. of Clinic. Pharmacol./Therap., Ninewells Hosp. and Medical School, Dundee DD1 9SY, United Kingdom. b.j.lipworth@dundee.ac.uk
SOURCE: Thorax, (2000) Vol. 55, No. 10, pp. 878-881. Refs: 36
ISSN: 0040-6376 CODEN: THORA7

COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; General Review; (Review)
FILE SEGMENT: 011 Otorhinolaryngology
015 Chest Diseases, Thoracic Surgery and Tuberculosis
037 Drug Literature Index
LANGUAGE: English
ENTRY DATE: Entered STN: 26 Oct 2000
Last Updated on STN: 26 Oct 2000
TI Allergic inflammation in the unified airway: Start with the nose.
RN (beclometasone) 4419-39-0; (budesonide) 51333-22-3; (cetirizine) 83881-51-0, 83881-52-1; (loratadine) 79794-75-5; (montelukast) 151767-02-1, 158966-92-8; (zafirlukast) 107753-78-6

L21 ANSWER 95 OF 100 EMBASE COPYRIGHT (c) 2008 Elsevier B.V. All rights reserved on STN
ACCESSION NUMBER: 2000198310 EMBASE <<LOGINID::20080303>>
TITLE: Allergic rhinitis.
AUTHOR: Virant F.S.
CORPORATE SOURCE: Dr. F.S. Virant, Northwest Asthma and Allergy Center, 4540 Sand Point Way NE, Seattle, WA 98105, United States
SOURCE: Immunology and Allergy Clinics of North America, (2000) Vol. 20, No. 2, pp. 265-282.
Refs: 62
ISSN: 0889-8561 CODEN: INCAEP
COUNTRY: United States
DOCUMENT TYPE: Journal; General Review; (Review)
FILE SEGMENT: 005 General Pathology and Pathological Anatomy
039 Pharmacy
038 Adverse Reactions Titles
037 Drug Literature Index
036 Health Policy, Economics and Management
026 Immunology, Serology and Transplantation
011 Otorhinolaryngology
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 30 Jun 2000
Last Updated on STN: 30 Jun 2000
AB . . . may play a primary pathophysiologic role in otitis media, sinusitis, and asthma. These secondary disorders occur because of upper airway inflammation and the release of various vasoactive mediators, including histamine, prostaglandins, and leukotrienes. The management of allergic rhinitis includes environmental controls,. . .
RN (astemizole) 68844-77-9; (azelastine) 58581-89-8, 79307-93-0; (beclometasone) 4419-39-0; (brompheniramine) 86-22-6, 980-71-2; (budesonide) 51333-22-3; (cetirizine) 83881-51-0, 83881-52-1; (chlorpheniramine) 132-22-9; (clemastine) 15686-51-8; (cromoglycate disodium) 15826-37-6, 16110-51-3, 93356-79-7, 93356-84-4; (cyproheptadine) 129-03-3, 969-33-5; (diphenhydramine) 147-24-0, 58-73-1; (fexofenadine) 138452-21-8; (flunisolide) 3385-03-3; (fluticasone) 90566-53-3; (histamine) 51-45-6, 56-92-8, 93443-21-1; (hydroxyzine) 2192-20-3, 64095-02-9, 68-88-2; (immunoglobulin E) 37341-29-0; (loratadine) 79794-75-5; (mometasone furoate) 83919-23-7; (terfenadine) 50679-08-8; (triamcinolone) 124-94-7; (tripelennamine) 154-69-8, 91-81-6; (triprolidine) 486-12-4, 550-70-9;

(zileuton) 111406-87-2, 132880-11-6

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ACCESSION NUMBER: 1999303030 EMBASE <<LOGINID::20080303>>
TITLE: [Histamine and leukotrienes in allergic rhinitis]. HISTAMIN UND LEUKOTRIENE BEI DER ALLERGISCHEN RHINITIS.
AUTHOR: Bachert C.; Lange B.
CORPORATE SOURCE: C. Bachert, Kliniek Neus-, Keel- en Oorheelkunde, UZ Gent, De Pintelaan 185, B-9000 Gent, Belgium
SOURCE: Allergologie, (Aug 1999) Vol. 22, No. 8, pp. 492-507. Refs: 105
ISSN: 0344-5062 CODEN: ALLRDI
COUNTRY: Germany
DOCUMENT TYPE: Journal; General Review; (Review)
FILE SEGMENT: 011 Otorhinolaryngology
026 Immunology, Serology and Transplantation
030 Clinical and Experimental Pharmacology
037 Drug Literature Index
LANGUAGE: German
SUMMARY LANGUAGE: English; German
ENTRY DATE: Entered STN: 10 Sep 1999
Last Updated on STN: 10 Sep 1999
AB . . . or eosinophils, and mechanisms like the adhesion cascade. This has led to the realization that allergic rhinitis is a persistent inflammation. While histamine is still considered the most important mediator of early phase reaction and mainly responsible for the symptoms sneezing,. . .
RN. . . 3 hydroxy 2 propylphenoxy)propylthio]phenyl] 4 hydroxy 3 methylbutyric acid) 91542-58-4; (alpha methyl 6 (2 quinolylmethoxy) 2 naphthylacetic acid) 133304-99-1; (azelastine) 58581-89-8, 79307-93-0; (budesonide) 51333-22-3; (cetirizine) 83881-51-0, 83881-52-1; (docebenone) 80809-81-0; (ebastine) 90729-43-4; (leukotriene B4) 71160-24-2; (leukotriene C4) 72025-60-6; (leukotriene D4) 73836-78-9; (leukotriene E4) 75715-89-8; (loratadine) 79794-75-5; (mizolastine) 108612-45-9; (montelukast) 151767-02-1, 158966-92-8; (piriprost) 79672-88-1; (pobilukast) 107023-41-6, 108116-15-0; (pranlukast) 103177-37-3; (terfenadine) 50679-08-8; (verlukast) 115104-28-4; (zafirlukast) 107753-78-6; (zileuton) 111406-87-2, 132880-11-6

L21 ANSWER 97 OF 100 EMBASE COPYRIGHT (c) 2008 Elsevier B.V. All rights reserved on STN
ACCESSION NUMBER: 1999174097 EMBASE <<LOGINID::20080303>>
TITLE: American Academy of Asthma, Allergy and Immunology - 55th Annual Meeting: 26 February - 3 March 1999, Orlando, FL, USA.
AUTHOR: Lieberman P.
CORPORATE SOURCE: P. Lieberman, Division of Allergy and Immunology, Univ. of Tennessee Coll. of Medicine, 300 Walnut Bend Road 50, Cordova, TN 38018, United States. asthmamemphis@msn.com
SOURCE: IDrugs, (1999) Vol. 2, No. 5, pp. 405-409.
ISSN: 1369-7056 CODEN: IDRUFN
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; Conference Article; (Conference paper)
FILE SEGMENT: 015 Chest Diseases, Thoracic Surgery and Tuberculosis

030 Clinical and Experimental Pharmacology
037 Drug Literature Index
038 Adverse Reactions Titles
007 Pediatrics and Pediatric Surgery
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 10 Jun 1999
Last Updated on STN: 10 Jun 1999
AB . . . 984 original oral and poster presentations and over 100 symposia, seminars and workshops. The plenary sessions involved sections on allergic inflammation, immune modulation, chemokine receptors, the origins of asthma, the diagnosis and management of food and drug reactions, the environmental influences. . .
RN (4 [2 [3 (cyclopentyloxy) 4 methoxyphenyl] 2 phenylethyl]pyridine) 162542-90-7; (azelastine) 58581-89-8, 79307-93-0; (beclometasone dipropionate) 5534-09-8; (budesonide) 51333-22-3; (cetirizine) 83881-51-0, 83881-52-1; (cilomilast) 153259-65-5; (cromoglycate disodium) 15826-37-6, 16110-51-3, 93356-79-7, 93356-84-4; (ebastine) 90729-43-4; (epinastine) 80012-43-7; (fexofenadine) 138452-21-8; (fluticasone propionate) 80474-14-2; (fluticasone) 90566-53-3; (loratadine) 79794-75-5; (montelukast) 151767-02-1, 158966-92-8; (piclamilast) 144035-83-6; (rapamycin) 53123-88-9; (recombinant intercellular adhesion molecule 1) 155576-45-7; (rolipram) 61413-54-5; (salbutamol) 18559-94-9; (salmeterol) 89365-50-4; (seratrodast) 103186-19-2, 112665-43-7; (terfenadine) 50679-08-8; (zafirlukast) 107753-78-6

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ACCESSION NUMBER: 1997186601 EMBASE <<LOGINID::20080303>>
TITLE: Asthma, allergic inflammation and new therapeutic strategies.
AUTHOR: Ciprandi G.
SOURCE: Drug News and Perspectives, (1997) Vol. 10, No. 3, pp. 161-165.
ISSN: 0214-0934 CODEN: DNPEED
COUNTRY: Spain
DOCUMENT TYPE: Journal; Conference Article; (Conference paper)
FILE SEGMENT: 015 Chest Diseases, Thoracic Surgery and Tuberculosis
026 Immunology, Serology and Transplantation
037 Drug Literature Index
LANGUAGE: English
ENTRY DATE: Entered STN: 10 Jul 1997
Last Updated on STN: 10 Jul 1997
TI Asthma, allergic inflammation and new therapeutic strategies.
RN (azelastine) 58581-89-8, 79307-93-0; (beclometasone dipropionate) 5534-09-8; (budesonide) 51333-22-3; (cromoglycate disodium) 15826-37-6, 16110-51-3, 93356-79-7, 93356-84-4; (fexofenadine) 138452-21-8; (fluticasone) 90566-53-3; (ipratropium bromide) 22254-24-6; (loratadine) 79794-75-5; (mometasone furoate) 83919-23-7; (nedocromil) 69049-73-6; (prednisone) 53-03-2; (triamcinolone acetonide) 76-25-5; (zafirlukast) 107753-78-6; (zanamivir) 139110-80-8; (zileuton) 111406-87-2, 132880-11-6

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ACCESSION NUMBER: 1996203538 EMBASE <<LOGINID::20080303>>
TITLE: Prospects for the development of new drugs for the therapy of respiratory diseases.
AUTHOR: Whelan C.J.
CORPORATE SOURCE: C.J. Whelan, Division of Biosciences, School of Natural Sciences, University of Hertfordshire, Hatfield, Herts AL10 9AB, United Kingdom
SOURCE: Drugs of Today, (1996) Vol. 32, No. 4, pp. 295-311.
Refs: 133
ISSN: 0025-7656 CODEN: MDACAP
COUNTRY: Spain
DOCUMENT TYPE: Journal; General Review; (Review)
FILE SEGMENT: 015 Chest Diseases, Thoracic Surgery and Tuberculosis
030 Clinical and Experimental Pharmacology
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 21 Aug 1996
Last Updated on STN: 21 Aug 1996
AB . . . or inhibitors of neutrophil recruitment and activation should offer an approach to the design of drugs which selectively target the inflammation associated with these diseases.
RN (apafant) 105219-56-5; (azelastine) 58581-89-8, 79307-93-0; (beclometasone dipropionate) 5534-09-8; (cetirizine) 83881-51-0, 83881-52-1; (cromakalim) 94470-67-4; (fluticasone propionate) 80474-14-2; (formoterol) 73573-87-2; (interleukin 8) 114308-91-7; (ipratropium bromide) 22254-24-6; (mifepristone) 84371-65-3; (modipafant) 122956-68-7; (salbutamol) 18559-94-9; (salmeterol) 89365-50-4; (siguazodan) 115344-47-3; (terbutaline) 23031-25-6; (theophylline) 58-55-9, 5967-84-0, 8055-07-0, 8061-56-1, 99007-19-9; (vapiprost) 85505-64-2; (zafirlukast) 107753-78-6; (zardaverine) 101975-10-4

L21 ANSWER 100 OF 100 EMBASE
ACCESSION NUMBER: 1992359918 EMBASE <<LOGINID::20080303>>
TITLE: Atopic disease in children.
AUTHOR: Bocian R.C.; Umetsu D.T.
CORPORATE SOURCE: Dr. R.C. Bocian, Division of Allergy, Department of Pediatrics, Stanford University Medical Center, Stanford, CA 94305-5119, United States
SOURCE: Current Opinion in Pediatrics, (1992) Vol. 4, No. 6, pp. 1008-1016.
ISSN: 1040-8703 CODEN: COPEE9
COUNTRY: United States
DOCUMENT TYPE: Journal; General Review; (Review)
FILE SEGMENT: 015 Chest Diseases, Thoracic Surgery and Tuberculosis
026 Immunology, Serology and Transplantation
037 Drug Literature Index
038 Adverse Reactions Titles
007 Pediatrics and Pediatric Surgery
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 10 Jan 1993
Last Updated on STN: 10 Jan 1993
CT Medical Descriptors:
*allergic . . . DT, drug therapy

*atopy: ET, etiology
bronchus reactivity
cigarette smoking
drug efficacy
drug safety
eosinophil
*food allergy: DT, drug therapy
*food allergy: ET, etiology
human
hypertension: SI, side effect
immunoglobulin blood level
immunotherapy
  inflammation: DT, drug therapy
  inflammation: ET, etiology
inhalational drug administration
intravenous drug administration
liver toxicity: SI, side effect
mast cell degranulation
mite
nephrotoxicity: SI, side effect
prick test
review
T lymphocyte
adrenalin: AD, drug. . .

RN (adrenalin) 51-43-4, 55-31-2, 6912-68-1; (aminophylline) 317-34-0; (azelastine) 58581-89-8, 79307-93-0; (beclometasone dipropionate) 5534-09-8; (budesonide) 51333-22-3; (cetirizine) 83881-51-0, 83881-52-1; (cromoglycate disodium) 15826-37-6, 16110-51-3, 93356-79-7, 93356-84-4; (cyclosporin A) 59865-13-3, 63798-73-2; (fenoterol) 13392-18-2, 1944-12-3; (gamma interferon) 82115-62-6; (immunoglobulin E) 37341-29-0; (immunoglobulin) 9007-83-4; (ketotifen) 34580-13-7; (methotrexate) 15475-56-6, 59-05-2, 7413-34-5; (methylprednisolone) 6923-42-8, 83-43-2; (nedocromil) 69049-73-6; (orciprenaline) 586-06-1, 5874-97-5; (pobilukast) 107023-41-6, 108116-15-0; (terbutaline) 23031-25-6; (theophylline) 58-55-9, 5967-84-0, 8055-07-0, 8061-56-1, 99007-19-9

=> d his

(FILE 'HOME' ENTERED AT 08:55:09 ON 03 MAR 2008)

FILE 'REGISTRY' ENTERED AT 08:55:39 ON 03 MAR 2008

L1 0 S MONTLUKAST/CN
L2 1 S MONTELUKAST/CN
L3 1 S ZILEUTON/CN
L4 1 S ZAFIRLUKAST/CN
L5 4 S ?LUKAST
L6 1 S FLUTICASONE PROPIONATE/CN
L7 0 S MOMETASONE FUORATE MONOHYDRATE/CN
L8 1 S MOMETASONE/CN
L9 1 S BUDESONIDE/CN
L10 1 S AZELASTINE/CN
L11 1 S CETIRIZINE/CN
L12 6 S FEXOFENADINE
L13 2 S LORATADINE

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L14           2 S DESLORATADINE

     FILE 'ADISCTI, ADISINSIGHT, ADISNEWS, BIOSIS, BIOTECHNO, CAPLUS, DDFB,
     DGENE, DISSABS, DRUGB, DRUGMONOG2, DRUGU, EMBAL, EMBASE, ESBIOBASE,
     IFIPAT, IMSDRUGNEWS, IMSPRODUCT, IPA, KOSMET, LIFESCI, MEDLINE,
     NAPRALERT, NLDB, NUTRACEUT, PASCAL, PCTGEN, PHARMAML, ...' ENTERED AT
     09:06:08 ON 03 MAR 2008
L15       11824 S L2 OR L3 OR L4 OR L5
L16       32489 S L6 OR L8 OR L9
L17       32316 S L10 OR L11 OR L12 OR L13 OR L14
L18     2287254 S C REACTIVE PROTEIN OR INFLAMMATION
L19         420 S L15 AND L16 AND L17
L20         128 S L18 AND L19
L21         100 DUP REM L20 (28 DUPLICATES REMOVED)

=> s c reactive protein
   8 FILES SEARCHED...
  33 FILES SEARCHED...
L22      161485 C REACTIVE PROTEIN

=> s l21 and l22

  35 FILES SEARCHED...
L23          10 L21 AND L22

=> d l23 1-10 ibib, kwic

L23  ANSWER 1 OF 10  CAPLUS  COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER:         2004:802553  CAPLUS <<LOGINID::20080303>>
DOCUMENT NUMBER:          141:289088
TITLE:                    Protocol for improving vision
INVENTOR(S):              Mullally, John P.
PATENT ASSIGNEE(S):       USA
SOURCE:                   U.S. Pat. Appl. Publ., 5 pp., Cont.-in-part of U.S.
                          Ser. No. 798,017.
                          CODEN: USXXCO
DOCUMENT TYPE:            Patent
LANGUAGE:                 English
FAMILY ACC. NUM. COUNT:   2
PATENT INFORMATION:

     PATENT NO.           KIND   DATE        APPLICATION NO.         DATE
     ---------------      ----   --------    --------------------    --------
     US 2004192660         A1    20040930    US 2004-820264          20040408
     CA 2518409            A1    20040923    CA 2004-2518409         20040311
     CA 2559276            A1    20050929    CA 2005-2559276         20050311
     WO 2005089171         A2    20050929    WO 2005-US7804          20050311
     WO 2005089171         A3    20060209
         W:  AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH,
             CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD,
             GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC,
             LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI,
             NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM,
             SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
         RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE,
             IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF,
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CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

PRIORITY APPLN. INFO.:

US 2003-453917P	P	20030312
US 2003-461534P	P	20030409
US 2003-482574P	P	20030624
US 2004-798017	A2	20040311
WO 2004-US7381	W	20040311
WO 2005-US7804	W	20050311

AB A method and composition for reducing highly sensitive C-reactive protein to improve the vision of a user is achieved through the daily administration of a leukotriene inhibitor, and antihistamine and. . .

IT Vision
(agents to improve; method and composition for reducing highly sensitive C-reactive protein to improve the vision)

IT Mycobacterium tuberculosis
(attenuated; method and composition for reducing highly sensitive C-reactive protein to improve the vision)

IT Drug delivery systems
(capsules; method and composition for reducing highly sensitive C-reactive protein to improve the vision)

IT Streptococcus pneumoniae
(conjugate vaccine; method and composition for reducing highly sensitive C-reactive protein to improve the vision)

IT Polysaccharides, biological studies
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(conjugates, pneumococcal; method and composition for reducing highly sensitive C-reactive protein to improve the vision)

IT Drug delivery systems
(infusions, nasal; method and composition for reducing highly sensitive C-reactive protein to improve the vision)

IT Antihistamines
Combination chemotherapy
Diabetes mellitus
Eye, disease
Human
Influenza virus
Mixtures
Vaccines
(method and composition for reducing highly sensitive C-reactive protein to improve the vision)

IT C-reactive protein
Leukotrienes
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(method and composition for reducing highly sensitive C-reactive protein to improve the vision)

IT Corticosteroids, biological studies
Steroids, biological studies
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(method and composition for reducing highly sensitive C-reactive protein to improve the vision)

IT Drug delivery systems

(nasal, infusion; method and composition for reducing highly sensitive C-reactive protein to improve the vision)
IT Drug delivery systems
(oral; method and composition for reducing highly sensitive C-reactive protein to improve the vision)
IT 51-30-9, Isoproterenol hydrochloride 53-03-2, Prednisone 54-11-5, Nicotine 54-85-3, Isoniazid 58-55-9, Theophylline, biological studies 61-72-3, Cloxacillin 69-53-4, Ampicillin 74-55-5, Ethambutol 76-25-5, Triamcinolone acetonide 98-96-4, Pyrazinamide 114-07-8, Erythromycin 317-34-0, Aminophylline 564-25-0, Doxycycline 586-06-1, Orciprenaline 1400-61-9, Nystatin 1406-05-9, Penicillin 1944-12-3, Fenoterol hydrobromide 3385-03-3, Flunisolide 4499-40-5, Oxtriphylline, biological studies 5534-09-8, Beclomethasone dipropionate 10118-90-8, Minocycline 13292-46-1, Rifampin 15686-71-2, Cephalexin 15826-37-6, Sodium cromoglycate 18323-44-9, Clindamycin 18559-94-9, Salbutamol 22254-24-6, Ipratropium bromide 23031-32-5, Terbutaline sulfate 26787-78-0, Amoxicillin 31677-93-7, Bupropion hydrochloride 33817-20-8, Pivampicillin 34580-13-7, Ketotifen 43229-80-7, Formoterol fumarate 50370-12-2, Cefadroxil 50679-08-8, Terfenadine 50972-17-3, Bacampicillin 51022-70-9, Albuterol sulfate 51333-22-3, Budesonide 53994-73-3, Cefaclor 58581-89-8, Azelastine 64544-07-6, Cefuroxime axetil 65277-42-1, Ketoconazole 65652-44-0, Pirbuterol acetate 68844-77-9, Astemizole 69049-74-7, Nedocromil sodium 79350-37-1, Cefixime 79794-75-5, Loratadine 80474-14-2, Fluticasone propionate 81103-11-9, Clarithromycin 82419-36-1, Ofloxacin 83799-24-0, Fexofenadine 83881-51-0, Cetirizine 83905-01-5, Azithromycin 84625-61-6, Itraconazole 86386-73-4, Fluconazole 92665-29-7, Cefprozil 93107-08-5, Ciprofloxacin hydrochloride 94749-08-3, Salmeterol xinafoate 100986-85-4, Levofloxacin 107753-78-6, Zafirlukast 112811-59-3, Gatifloxacin 139110-80-8, Zanamivir 141646-00-6, Mometasone furoate monohydrate 151096-09-2, Moxifloxacin 151767-02-1, Montelukast sodium 196618-13-0, Oseltamivir 756819-03-1
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(method and composition for reducing highly sensitive C-reactive protein to improve the vision)

L23 ANSWER 2 OF 10 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2004:759824 CAPLUS <<LOGINID::20080303>>
DOCUMENT NUMBER: 141:254560
TITLE: Composition and method using a leukotriene inhibitor, an antihistamine and a corticosteroid for treating inflammation by reducing C-reactive protein
INVENTOR(S): Mullally, John P.
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 8 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE

US 2004180868 A1 20040916 US 2004-798117 20040311
CA 2518409 A1 20040923 CA 2004-2518409 20040311
WO 2004080414 A2 20040923 WO 2004-US7381 20040311
WO 2004080414 A3 20050512
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
PRIORITY APPLN. INFO.: US 2003-453917P P 20030312
US 2003-482574P P 20030624
WO 2004-US7381 W 20040311

TI Composition and method using a leukotriene inhibitor, an antihistamine and a corticosteroid for treating inflammation by reducing C -reactive protein

AB A method and composition for reducing C-reactive protein for reducing systemic inflammation in the body of a user is achieved through the daily administration of a leukotriene inhibitor, an antihistamine, and a. . .

ST leukotriene inhibitor antihistamine corticosteroid inflammation treatment C reactive protein

IT Mycobacterium tuberculosis
(attenuated; leukotriene inhibitor, antihistamine, and corticosteroid for treating inflammation by reducing C-reactive protein)

IT Vaccines
(influenza virus; leukotriene inhibitor, antihistamine, and corticosteroid for treating inflammation by reducing C-reactive protein)

IT Drug delivery systems
(infusions; leukotriene inhibitor, antihistamine, and corticosteroid for treating inflammation by reducing C-reactive protein)

IT Anti-inflammatory agents
Antihistamines
Combination chemotherapy
Drug delivery systems
Human
Inflammation
(leukotriene inhibitor, antihistamine, and corticosteroid for treating inflammation by reducing C-reactive protein)

IT C-reactive protein
Glycerides, biological studies
High-density lipoproteins
Leukotrienes
Low-density lipoproteins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(leukotriene inhibitor, antihistamine, and corticosteroid for treating inflammation by reducing C-reactive

protein)
IT Corticosteroids, biological studies
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(leukotriene inhibitor, antihistamine, and corticosteroid for treating inflammation by reducing C-reactive protein)
IT Drug delivery systems
(nasal; leukotriene inhibitor, antihistamine, and corticosteroid for treating inflammation by reducing C-reactive protein)
IT Drug delivery systems
(oral; leukotriene inhibitor, antihistamine, and corticosteroid for treating inflammation by reducing C-reactive protein)
IT Streptococcus pneumoniae
(pneumococcal conjugate vaccine; leukotriene inhibitor, antihistamine, and corticosteroid for treating inflammation by reducing C-reactive protein)
IT Polysaccharides, biological studies
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(pneumococcal polysaccharide vaccine; leukotriene inhibitor, antihistamine, and corticosteroid for treating inflammation by reducing C-reactive protein)
IT Inflammation
Respiratory system, disease
(sinusitis; leukotriene inhibitor, antihistamine, and corticosteroid for treating inflammation by reducing C-reactive protein)
IT Influenza virus
(vaccine; leukotriene inhibitor, antihistamine, and corticosteroid for treating inflammation by reducing C-reactive protein)
IT 57-88-5, Cholesterol, biological studies 9004-10-8, Insulin, biological studies 62572-11-6, Hemoglobin A1c
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(leukotriene inhibitor, antihistamine, and corticosteroid for treating inflammation by reducing C-reactive protein)
IT 51-30-9, Isoproterenol hydrochloride 53-03-2, Prednisone 54-11-5, Nicotine 54-31-9, Lasix 54-85-3, Isoniazid 58-55-9, Theophylline, biological studies 61-72-3, Cloxacillin 69-53-4, Ampicillin 74-55-5, Ethambutol 76-25-5, Triamcinolone acetonide 98-96-4, Pyrazinamide 114-07-8, Erythromycin 317-34-0, Aminophylline 564-25-0, Doxycycline 586-06-1, Orciprenaline 1400-61-9, Nystatin 1406-05-9, Penicillin 1944-12-3, Fenoterol hydrobromide 3385-03-3, Flunisolide 4499-40-5, Oxtriphylline, biological studies 5534-09-8, Beclomethasone dipropionate 10118-90-8, Minocycline 13292-46-1, Rifampin 15686-71-2, Cephalexin 15826-37-6, Sodium cromoglycate 18323-44-9, Clindamycin 18559-94-9, Salbutamol 22254-24-6, Ipratropium bromide 23031-32-5, Terbutaline sulfate 26787-78-0, Amoxicillin 31677-93-7, Bupropion hydrochloride 33817-20-8, Pivampicillin 34580-13-7, Ketotifen 43229-80-7, Formoterol fumarate 50370-12-2, Cefadroxil 50679-08-8, Terfenadine 50972-17-3, Bacampicillin 51022-70-9, Albuterol sulfate 51333-22-3, Budesonide 53994-73-3, Cefaclor 58581-89-8, Azelastine.

64544-07-6, Cefuroxime axetil 65277-42-1, Ketoconazole 65652-44-0, Pirbuterol acetate 68844-77-9, Astemizole 69049-74-7, Nedocromil sodium 79307-93-0, Astelin 79350-37-1, Cefixime 79794-75-5, Loratadine 79902-63-9, Zocor 80474-14-2, Fluticasone propionate 81103-11-9, Clarithromycin 82419-36-1, Ofloxacin 83799-24-0, Fexofenadine 83881-51-0, Cetirizine 83905-01-5, Azithromycin 84625-61-6, Itraconazole 86386-73-4, Fluconazole 92665-29-7, Cefprozil 93107-08-5, Ciprofloxacin hydrochloride 94749-08-3, Salmeterol xinafoate 100986-85-4, Levofloxacin 105816-04-4, Starlix 107133-36-8, Aceon 107753-78-6, Zafirlukast 112811-59-3, Gatifloxacin 135062-02-1, Prandin 139110-80-8, Zanamivir 141646-00-6, Mometasone furoate monohydrate 151096-09-2, Moxifloxacin 151767-02-1, Montelukast sodium 153439-40-8, Allegra 155141-29-0, Avandia 156154-37-9, Hyzaar 196618-13-0, Oseltamivir 338752-31-1, Glucovance 756819-03-1
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(leukotriene inhibitor, antihistamine, and corticosteroid for treating inflammation by reducing C-reactive protein)

L23 ANSWER 3 OF 10 USPATFULL on STN

ACCESSION NUMBER:	2007:184688 USPATFULL <<LOGINID::20080303>>
TITLE:	ETHER DERIVATIVES USEFUL AS INHIBITORS OF PDE4 ISOZYMES
INVENTOR(S):	Marfat, Anthony, 333 Lantern Hill Road, Mystic, CT, UNITED STATES 06378 Chambers, Robert J., 25 Clipper Drive, Mystic, CT, UNITED STATES 06355 Magee, Thomas V., 1288 River Road, Mystic, CT, UNITED STATES 06355
PATENT ASSIGNEE(S):	PFIZER INC., New York, NY, UNITED STATES, 10017-5755 (U.S. corporation) PFIZER PRODUCTS INC., Groton, CT, UNITED STATES, 06340 (U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2007161681	A1	20070712
APPLICATION INFO.:	US 2007-668915	A1	20070130 (11)

RELATED APPLN. INFO.:	Division of Ser. No. US 2004-918820, filed on 13 Aug 2004, GRANTED, Pat. No. US 7183293 Division of Ser. No. US 2002-66503, filed on 31 Jan 2002, GRANTED, Pat. No. US 6828333

	NUMBER	DATE
PRIORITY INFORMATION:	US 2001-265304P	20010131 (60)

DOCUMENT TYPE:	Utility
FILE SEGMENT:	APPLICATION
LEGAL REPRESENTATIVE:	WARNER-LAMBERT COMPANY, 2800 PLYMOUTH RD, ANN ARBOR, MI, 48105, US
NUMBER OF CLAIMS:	30
EXEMPLARY CLAIM:	1
LINE COUNT:	7866

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

SUMM . . . for more selective inhibitors of PDEs that are able to suppress both immune cell functions in vitro and allergic pulmonary inflammation in vivo, while at the same time having improved side-effect profiles. Within the airways of patients suffering from asthma and. . .

SUMM Airflow obstruction and airway inflammation are features of asthma as well as COPD. While bronchial asthma is predominantly characterized by an eosinophilic inflammation, neutrophils appear to play a major role in the pathogenesis of COPb. Thus, PDEs that are involved in smooth muscle. . .

SUMM . . . hydrolases from their granules, and the generation of reactive oxygen species, neutrophils contribute to the tissue destruction associated with chronic inflammation, and are further implicated in the pathology of conditions such as emphysema.

SUMM . . . 400 mg; Pruniaux et at., "The novel phosphodiesterase inhibitor CI-1018 inhibits antigen-induced lung eosinophilia in sensitized brown-norway rats--comparison with rolipram," Inflammation S-04-6, 1999. CI-1018 has been demonstrated to have good oral bioavailability (57% in the rat) and good oral potency of. . .

SUMM . . . arthritis; infectious arthritis; Lyme arthritis; proliferative arthritis; psoriatic arthritis; and vertebral arthritis; gout, and fever and pain associated with inflammation; an eosinophil-related disorder of whatever type, etiology, or pathogenesis; or an eosinophil-related disorder that is a member selected from. . . uveitis of whatever type, etiology, or pathogenesis; or uveitis that is a member selected from the group consisting of inflammation of all or part of the uvea; anterior uveitis; iritis; cyclitis; iridocyclitis; granulomatous uveitis; nongranulomatous uveitis; phacoantigenic uveitis; posterior uveitis;. . .

SUMM In particular, the compounds of Formula (1.0.0) are useful in the treatment of (1) inflammatory diseases and conditions comprising: joint inflammation, rheumatoid arthritis, rheumatoid spondylitis, osteoarthritis, inflammatory bowel disease, ulcerative colitis, chronic glomerulonephritis, dermatitis, and Crohn's disease; (2) respiratory diseases and. . .

DETD . . . (1.0.0) is asthma, a chronic, increasingly common disorder encountered worldwide and characterized by intermittent reversible airway obstruction, airway hyper-responsiveness and inflammation . The cause of asthma has yet to be determined, but the most common pathological expression of asthma is inflammation of the airways, which may be significant even in the airways of patients with mild asthma. Based on bronchial biopsy. . .

DETD Pulmonary Inflammation in Allergic Cynomolgus Monkeys--The ability of the combinations of therapeutic agents of the present invention to inhibit Ascaris antigen induced. . .

DETD . . . use of primates, is that described in Turner et al., "Characterization of a primate model of asthma using anti-allergy/anti-asthma agents," Inflammation Research 45 239-245, 1996.

DETD COPD is characterized by inflammation of the airways, as is the case with asthma, but the inflammatory cells that have been found in the bronchoalveolar. . .

DETD . . . a productive cough; staphylococcus or streptococcal bronchitis which are caused by staphylococci or streptococci; and vesicular bronchitis in which the inflammation extends into the alveoli,

which are sometimes visible under the pleura as whitish-yellow granulations like millet seeds.

DETD . . . and T-lymphocytes. A variety of inflammatory mediators is also released by these cells, all of which may contribute to the inflammation exhibited in the late phase response.

DETD . . . al "Effect of AWD 12-281, a new selective PDE-4 inhibitor, loteprednol and beclomethasone in models of allergic rhinitis and airway inflammation in brown norway-rats," Am. J. Respir. Crit. Care Med. A95, 1999. The compounds D-22888 and AWD-12,281 have already been described. . .

DETD . . . rhinitis in terms of anatomical proximity as well as a shared etiology and pathogenesis in some cases. Sinusitis is the inflammation of a sinus and this condition may be purulent or nonpurulent, as well as acute or chronic. Depending upon the sinus where the inflammation is located, the condition is known as ethmoid, frontal, maxillary, or sphenoid sinusitis. The ethmoidal sinus is one type of. . .

DETD Arthritis is defined as inflammation of the joints, and rheumatoid arthritis is a chronic systemic disease primarily of the joints, usually polyarticular, marked by inflammatory. . .

DETD . . . Accordingly, the term "rheumatoid arthritis" includes acute arthritis, which is arthritis marked by pain, heat, redness, and swelling due to inflammation, infection, or trauma; acute gouty arthritis, which is acute arthritis associated with gout; chronic inflammatory arthritis, which is inflammation of the joints in chronic disorders such as rheumatoid arthritis; degenerative arthritis, which is osteoarthritis; infectious arthritis, which is arthritis. . . or parasites; Lyme arthritis, which is arthritis of the large joints associated with Lyme 20 disease; proliferative arthritis, which is inflammation of the joints with proliferation of the synovium, seen in rheumatoid arthritis; psoriatic arthritis, which is a syndrome in which psoriasis occurs in association with inflammatory arthritis; and vertebral arthritis, which is inflammation involving the intervertebral disks.

DETD The three major pathological features of rheumatoid arthritis that are responsible for progressive joint destruction are inflammation , abnormal cellular and humoral responses, and synovial hyperplasia. The particular cellular pathology of rheumatoid arthritis includes the presence of T-cells. . . disease. Pro-inflammatory cytokines, e.g., IL-1, IL-4, IL-5, IL-6, IL-9, IL-13, and TNF-α, are the major contributors to joint tissue damage, inflammation, hyperplasia, pannus formation and bone resorption. See Firestein, G. S. and Zvaifier, W. J., "How important are T-cells in chronic. . .

DETD . . . of the compounds of Formula (1.0.0) to inhibit TNF-α release from stimulated monocytes can be correlated with animal models of inflammation in which anti-inflammatory effects can be shown to correspond to suppression of TNF-α accumulation. One such animal model involves inhibition. . .

DETD . . . are tophi or chalky deposits of sodium urate. Some therapeutic agents are useful in treating both gout and its attendant inflammation, e.g., phenylbutazone and colchicine; while other therapeutic agents possess only uricosuric properties, e.g., sulfinpyrazone and benzbromarone

DETD . . . to the present invention such fever is either that manifested in pharyngoconjunctival fever or rheumatic fever, or that manifested during inflammation. A concomitant of inflammation

is pain, especially that experienced in the joints and connective tissue of those suffering from rheumatoid arthritis and gout.

DETD . . . PDE4 inhibitory compounds of Formula (1.0.0) provide beneficial results in the treatment of gout, and fever and pain associated with inflammation.

DETD . . . PDE4 inhibitors and their utility in the treatment of rheumatoid arthritis. The activity of rolipram in animal models of acute inflammation such as the mouse adjuvant arthritis model, has been demonstrated in the art; Sekut et al, "Anti-inflammatory activity of phosphodiesterase (PDE) IV inhibitors in acute and chronic models of inflammation," Olin. Exp. Immunol. 100(1) 126-132, 1995. The ability of rolipram to reduce disease severity in the collagen 11 induced arthritis. . .

DETD . . . the compound t.i.d. The compound was able to induce a positive trend towards clinical improvement associated with a reduction in C-reactive protein and IL-6 serum levels.
Chikanza et al, "The clinical effects of RP73401 phosphodiesterase Type 4 inhibitor in patients with rheumatoid. . .

DETD . . . a central role in the induction of local IgE responses and the recruitment of eosinophils in this disease. The chronic inflammation seen in atopic dermatitis is considered to be the result of several interdependent factors, such as repeated or persistent allergen. . . vascular adhesion molecule-1 (VCAM-1), an adhesion molecule involved in the migration of mononuclear cells and eosinophils into sites of tissue inflammation. Further, IL-5 is a key mediator of eosinophil activation, which is a common feature of atopic disease.

DETD . . . conjunctiva is a delicate membrane that lines the eyelids and covers the exposed surface of the sclera. Conjunctivitis is an inflammation of the conjunctiva that generally consists of conjunctival hyperemia associated with a discharge. The most common types of conjunctivitis, which. . . which is an acute conjunctivitis caused by bacteria or viruses, particularly gonococci, meningococci, pneumococci, and streptococci, and characterized by severe inflammation of the conjunctiva and copious discharge of pus; and vernal conjunctivitis which is a bilateral conjunctivitis of seasonal occurrence, of. . .

DETD . . . is the vascular middle coat or tunic of the eye, comprising the iris, ciliary body, and choroid. Uveitis is an inflammation of all or part of the uvea and commonly involves the other tunics of the eye, i.e., the sclera and. . . the posterior portion, characterized by nodular collections of epithelioid cells and giant cells surrounded by lymphocytes; nongranulomatous uveitis which is inflammation of the anterior portion of the uveal tract, i.e., the iris and ciliary body; phacoantigenic uveitis which is one of. . .

DETD . . . number of mediators via either topical or systemic administration. For example, rolipram has been shown to inhibit croton oil-induced ear inflammation in the mouse at topical doses as low as 0.03 mg per ear. The selective PDE4 inhibitor Ro 20-1724 has. . .

DETD A sclerosis is an induration, or hardening, and refers especially to hardening of a part from inflammation, and from increased formation of connective tissue and in diseases of the interstitial substance. The term "sclerosis" is used chiefly. . .

DETD Multiple sclerosis is an autoimmune disease that in addition to chronic inflammation and demyelination, also results in gliosis within

the central nervous system. There are several disease subtypes, including primary progressive multiple. . . subtypes may be distinguished from each other on the basis of the course of the disease, of the type of inflammation involved, and through the use of magnetic resonance imaging (MRI). It is also possible for the basic disease mechanism to change during the course of multiple sclerosis, with an inflammation-based process being replaced later by one which involves demyelination and axonal damage. See Weilbach and Gold, "Disease modifying treatments for. . .

DETD . . . compounds of Formula (1.0.0) also possess activity as immunosuppressive agents and are especially useful for treating autoimmune diseases in which inflammation is a component part of the autoimmune disease, or in which inflammation is part of the etiology of the autoimmune disease, or in which inflammation is otherwise involved with the autoimmune disease. Alternatively, the compounds of Formula (1.0.0) are anti-inflammatory agents useful in the treatment. . .

DETD . . . with the formation of pseudopolyps, i.e., edematous, inflamed islands of mucosa between areas of ulceration; and transmural colitis, which is inflammation of the full thickness of the bowel, rather than mucosal and submucosal disease, usually with the formation of noncaseating granulomas,. . .

DETD . . . arthritis; infectious arthritis; Lyme arthritis; proliferative arthritis; psoriatic arthritis; and vertebral arthritis; gout, and fever and pain associated with inflammation; an eosinophil-related disorder of whatever type, etiology, or pathogenesis; or an eosinophil-related disorder that is a member selected from. . . uveitis of whatever type, etiology, or pathogenesis; or uveitis that is a member selected from the group consisting of inflammation of all or part of the uvea; anterior uveitis; iritis; cyclitis; iridocyclitis; granulomatous uveitis; nongranulomatous uveitis; phacoantigenic uveitis; posterior uveitis;. . .

DETD . . . anesthetics for relieving pain, irritation and itching, e.g., benzocaine, lidocaine, dibucaine, and pramoxine hydrochloride; topical analgesics for relieving pain and inflammation, e.g., methyl salicylate, camphor, menthol, and resorcinol; topical antiseptics for preventing infection, e.g., benzalkonium chloride and povidone-iodine; and vitamins and. . .

CLM What is claimed is:

. . . degenerative arthritis; infectious arthritis; Lyme arthritis; proliferative arthritis; psoriatic arthritis; and vertebral arthritis; gout, and fever and pain associated with inflammation; an eosinophil-related disorder of whatever type, etiology, or pathogenesis; or an eosinophil-related disorder that is a member selected from the. . . conjunctivitis; uveitis of whatever type, etiology, or pathogenesis; or uveitis that is a member selected from the group consisting of inflammation of all or part of the uvea; anterior uveitis; iritis; cyclitis; iridocyclitis; granulomatous uveitis; nongranulomatous uveitis; phacoantigenic uveitis; posterior uveitis;. . .

. . . disease, disorder, or condition is a member selected from the group consisiting of (1) inflammatory diseases and conditions comprising: joint inflammation, rheumatoid arthritis, rheumatoid spondylitis, osteoarthritis, inflammatory bowel disease, ulcerative colitis, chronic glomerulonephritis, dermatitis, and Crohn's disease; (2) respiratory diseases and. . .

IT 50-24-8, Prednisolone 53-03-2, Prednisone 57-22-7, Vincristine

57-66-9, Probenecid 57-96-5, Sulfinpyrazone 58-55-9, Theophylline, biological studies 59-05-2, Methotrexate 59-42-7, Phenylephrine 64-86-8, Colchicine 76-25-5, Triamcinolone acetonide 90-82-4, Pseudoephedrine 101-40-6, Propylhexedrine 113-92-8, Chlorpheniramine 128-39-2D, 2,6-Di-tert-butylphenol, hydrazone derivs. 315-30-0, Allopurinol 317-34-0, Aminophylline 404-86-4, Capsaicin 446-86-6, Azathioprine 522-48-5, Tetrahydrozoline hydrochloride 550-99-2, Naphazoline hydrochloride 586-06-1, Metaproterenol 865-21-4, Vinblastine 1218-35-5, Xylometazoline hydrochloride 2315-02-8, Oxymetazoline hydrochloride 3198-07-0 3385-03-3, Flunisolide 3562-84-3, Benzbromarone 5534-09-8, Beclomethasone dipropionate 6339-87-3D, Thiophene-2-sulfonamide, derivs. 7440-57-5D, Gold, aurothio derivs. 7683-59-2, Isoproterenol 9004-08-4D, Cathepsin, derivs. 14838-15-4, Phenylpropanolamine 15826-37-6, Sodium cromoglycate 18559-94-9, Albuterol 22254-24-6, Ipratropium bromide 23031-25-6, Terbutaline 28797-61-7, Pirenzepine 30286-75-0, Oxitropium bromide 30392-40-6, Bitolterol 38677-81-5, Pirbuterol 51333-22-3, Budesonide 58581-89-8, Azelastine 59865-13-3, Cyclosporine 68844-77-9, Astemizole 73573-87-2, Formoterol 75706-12-6, Leflunomide 79794-75-5, Loratadine 80474-14-2, Fluticasone propionate 80880-90-6, Telenzepine 83799-24-0, Fexofenadine 83869-56-1, Granulocyte-macrophage colony-stimulating factor 83881-51-0, Cetirizine 83919-23-7, Mometasone furoate 89365-50-4, Salmeterol 93211-49-5, L-651392 96566-25-5, Ablukast 100643-71-8, Desloratadine 103177-37-3, Pranlukast 103475-41-8, Tepoxalin 106096-93-9, Basic fibroblast growth factor 107753-78-6, Zafirlukast 111406-87-2, Zileuton 118414-82-7, MK-886 120128-20-3, RG-12525 120443-16-5, Verlukast 126544-47-6, Ciclesonide 128253-31-6, BAY x 1005 128312-51-6 136310-93-5, Tiotropium bromide 140841-32-3 141579-54-6, Fenleuton 141579-87-5 143538-27-6, BAY x 7195 147030-01-1, MK-591 147398-01-4, CGS-25019c 147432-77-7, Ontazolast 151581-24-7, Iralukast 154355-76-7, ABT-761 158930-07-5, L-739010 158966-92-8, Montelukast 162011-90-7, Rofecoxib 162750-10-9, SB-210661 168154-07-2, L-746530 170277-31-3, Infliximab 171964-73-1, ZD-0892 174636-32-9, Talnetant 185243-69-0, Etanercept 202415-99-4 204974-93-6, BIIL 260 257892-34-5, D 4418 331731-18-1, D 2E7 346735-24-8, BIIL 284 350610-64-9, NKP-608C 446023-33-2, UT 77

(combination therapy with PDE4 inhibitors; preparation of carbamoyl-substituted pyridinyl aryl ether derivs. as inhibitors of PDE4 isoenzymes)

L23 ANSWER 4 OF 10 USPATFULL on STN

ACCESSION NUMBER: 2005:57341 USPATFULL <<LOGINID::20080303>>

TITLE: Ether derivatives useful as inhibitors of PDE4 isozymes

INVENTOR(S): Marfat, Anthony, Mystic, CT, UNITED STATES
Chambers, Robert J., Mystic, CT, UNITED STATES
Magee, Thomas V., Mystic, CT, UNITED STATES

PATENT ASSIGNEE(S): Pfizer Inc (U.S. corporation)

	NUMBER	KIND	DATE	
PATENT INFORMATION:	US 2005049258	A1	20050303	
	US 7183293	B2	20070227	
APPLICATION INFO.:	US 2004-918820	A1	20040813	(10)

RELATED APPLN. INFO.:	Division of Ser. No. US 2002-66503, filed on 31 Jan 2002, GRANTED, Pat. No. US 6828333	
	NUMBER	DATE
PRIORITY INFORMATION:	US 2001-265304P	20010131 (60)
DOCUMENT TYPE:	Utility	
FILE SEGMENT:	APPLICATION	
LEGAL REPRESENTATIVE:	PFIZER INC., PATENT DEPARTMENT, MS8260-1611, EASTERN POINT ROAD, GROTON, CT, 06340	
NUMBER OF CLAIMS:	9	
EXEMPLARY CLAIM:	1	
LINE COUNT:	7224	

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

SUMM . . . for more selective inhibitors of PDEs that are able to suppress both immune cell functions in vitro and allergic pulmonary inflammation in vivo, while at the same time having improved side-effect profiles. Within the airways of patients suffering from asthma and. . .

SUMM [0008] Airflow obstruction and airway inflammation are features of asthma as well as COPD. While bronchial asthma is predominantly characterized by an eosinophilic inflammation, neutrophils appear to play a major role in the pathogenesis of COPb. Thus, PDEs that are involved in smooth muscle. . .

SUMM . . . hydrolases from their granules, and the generation of reactive oxygen species, neutrophils contribute to the tissue destruction associated with chronic inflammation, and are further implicated in the pathology of conditions such as emphysema.

SUMM . . . 400 mg; Pruniaux et al., "The novel phosphodiesterase inhibitor Cl-1018 inhibits antigen-induced lung eosinophilia in sensitized brown-norway rats--comparison with rolipram," Inflammation S-04-6, 1999. Cl-1018 has been demonstrated to have good oral bioavailability (57% in the rat) and good oral potency of. . .

SUMM [0200] gout, and fever and pain associated with inflammation;

SUMM [0205] uveitis of whatever type, etiology, or pathogenesis; or uveitis that is a member selected from the group consisting of inflammation of all or part of the uvea; anterior uveitis; iritis; cyclitis; iridocyclitis; granulomatous uveitis; nongranulomatous uveitis; phacoantigenic uveitis; posterior uveitis;. . .

SUMM . . . In particular, the compounds of Formula (1.0.0) are useful in the treatment of (1) inflammatory diseases and conditions comprising: joint inflammation, rheumatoid arthritis, rheumatoid spondylitis, osteoarthritis, inflammatory bowel disease, ulcerative colitis, chronic glomerulonephritis, dermatitis, and Crohn's disease; (2) respiratory diseases and. . .

DETD . . . (1.0.0) is asthma, a chronic, increasingly common disorder encountered worldwide and characterized by intermittent reversible airway obstruction, airway hyper-responsiveness and inflammation . The cause of asthma has yet to be determined, but the most common pathological expression of asthma is inflammation of the airways, which may be significant even in the airways of patients with mild asthma. Based on bronchial biopsy. . .

DETD [0404] Pulmonary Inflammation in Allergic Cynomolgus Monkeys--The ability of the combinations of therapeutic agents of the present invention to inhibit Ascaris antigen induced. . .

DETD . . . use of primates, is that described in Turner et al.,

"Characterization of a primate model of asthma using anti-allergy/anti-asthma agents," Inflammation Research 45 239-245, 1996.

DETD [0419] COPD is characterized by inflammation of the airways, as is the case with asthma, but the inflammatory cells that have been found in the bronchoalveolar. . .

DETD . . . a productive cough; staphylococcus or streptococcal bronchitis which are caused by staphylococci or streptococci; and vesicular bronchitis in which the inflammation extends into the alveoli, which are sometimes visible under the pleura as whitish-yellow granulations like millet seeds.

DETD . . . and T-lymphocytes. A variety of inflammatory mediators is also released by these cells, all of which may contribute to the inflammation exhibited in the late phase response.

DETD . . . al "Effect of AWD 12-281, a new selective PDE-4 inhibitor, loteprednol and beclomethasone in models of allergic rhinitis and airway inflammation in brown norway-rats," Am. J. Respir. Crit. Care Med. A95, 1999. The compounds D-22888 and AWD-12,281 have already been described. . .

DETD . . . rhinitis in terms of anatomical proximity as well as a shared etiology and pathogenesis in some cases. Sinusitis is the inflammation of a sinus and this condition may be purulent or nonpurulent, as well as acute or chronic. Depending upon the sinus where the inflammation is located, the condition is known as ethmoid, frontal, maxillary, or sphenoid sinusitis. The ethmoidal sinus is one type of. . .

DETD [0441] Arthritis is defined as inflammation of the joints, and rheumatoid arthritis is a chronic systemic disease primarily of the joints, usually polyarticular, marked by inflammatory. . .

DETD . . . Accordingly, the term "rheumatoid arthritis" includes acute arthritis, which is arthritis marked by pain, heat, redness, and swelling due to inflammation, infection, or trauma; acute gouty arthritis, which is acute arthritis associated with gout; chronic inflammatory arthritis, which is inflammation of the joints in chronic disorders such as rheumatoid arthritis; degenerative arthritis, which is osteoarthritis; infectious arthritis, which is arthritis. . . or parasites; Lyme arthritis, which is arthritis of the large joints associated with Lyme 20 disease; proliferative arthritis, which is inflammation of the joints with proliferation of the synovium, seen in rheumatoid arthritis; psoriatic arthritis, which is a syndrome in which psoriasis occurs in association with inflammatory arthritis; and vertebral arthritis, which is inflammation involving the intervertebral disks.

DETD [0443] The three major pathological features of rheumatoid arthritis that are responsible for progressive joint destruction are inflammation, abnormal cellular and humoral responses, and synovial hyperplasia. The particular cellular pathology of rheumatoid arthritis includes the presence of T-cells. . . disease. Pro-inflammatory cytokines, e.g., IL-1, IL-4, IL-5, IL-6, IL-9, IL-13, and TNF-α, are the major contributors to joint tissue damage, inflammation, hyperplasia, pannus formation and bone resorption. See Firestein, G. S. and Zvaifier, W. J., "How important are T-cells in chronic. . .

DETD . . . of the compounds of Formula (1.0.0) to inhibit TNF-α release from stimulated monocytes can be correlated with animal models of inflammation in which anti-inflammatory effects can be

shown to correspond to suppression of TNF-α accumulation. One such animal model involves inhibition. . .

DETD . . . are tophi or chalky deposits of sodium urate. Some therapeutic agents are useful in treating both gout and its attendant inflammation, e.g., phenylbutazone and colchicine; while other therapeutic agents possess only uricosuric properties, e.g., sulfinpyrazone and benzbromarone

DETD . . . to the present invention such fever is either that manifested in pharyngoconjunctival fever or rheumatic fever, or that manifested during inflammation. A concomitant of inflammation is pain, especially that experienced in the joints and connective tissue of those suffering from rheumatoid arthritis and gout.

DETD . . . PDE4 inhibitory compounds of Formula (1.0.0) provide beneficial results in the treatment of gout, and fever and pain associated with inflammation.

DETD . . . PDE4 inhibitors and their utility in the treatment of rheumatoid arthritis. The activity of rolipram in animal models of acute inflammation such as the mouse adjuvant arthritis model, has been demonstrated in the art; Sekut et al, "Anti-inflammatory activity of phosphodiesterase (PDE) IV inhibitors in acute and chronic models of inflammation," Olin. Exp. Immunol. 100(1) 126-132, 1995. The ability of rolipram to reduce disease severity in the collagen 11 induced arthritis. . .

DETD . . . the compound t.i.d. The compound was able to induce a positive trend towards clinical improvement associated with a reduction in C-reactive protein and IL-6 serum levels.
Chikanza et al, "The clinical effects of RP73401 phosphodiesterase Type 4 inhibitor in patients with rheumatoid. . .

DETD . . . a central role in the induction of local IgE responses and the recruitment of eosinophils in this disease. The chronic inflammation seen in atopic dermatitis is considered to be the result of several interdependent factors, such as repeated or persistent allergen. . . vascular adhesion molecule-1 (VCAM-1), an adhesion molecule involved in the migration of mononuclear cells and eosinophils into sites of tissue inflammation. Further, IL-5 is a key mediator of eosinophil activation, which is a common feature of atopic disease.

DETD . . . conjunctiva is a delicate membrane that lines the eyelids and covers the exposed surface of the sclera. Conjunctivitis is an inflammation of the conjunctiva that generally consists of conjunctival hyperemia associated with a discharge. The most common types of conjunctivitis, which. . . which is an acute conjunctivitis caused by bacteria or viruses, particularly gonococci, meningococci, pneumococci, and streptococci, and characterized by severe inflammation of the conjunctiva and copious discharge of pus; and vernal conjunctivitis which is a bilateral conjunctivitis of seasonal occurrence, of. . .

DETD . . . is the vascular middle coat or tunic of the eye, comprising the iris, ciliary body, and choroid. Uveitis is an inflammation of all or part of the uvea and commonly involves the other tunics of the eye, i.e., the sclera and. . . the posterior portion, characterized by nodular collections of epithelioid cells and giant cells surrounded by lymphocytes; nongranulomatous uveitis which is inflammation of the anterior portion of the uveal tract, i.e., the iris and ciliary body; phacoantigenic uveitis which is one of. . .

DETD . . . number of mediators via either topical or systemic

administration. For example, rolipram has been shown to inhibit croton oil-induced ear inflammation in the mouse at topical doses as low as 0.03 mg per ear. The selective PDE4 inhibitor Ro 20-1724 has. . .

DETD [0474] A sclerosis is an induration, or hardening, and refers especially to hardening of a part from inflammation, and from increased formation of connective tissue and in diseases of the interstitial substance. The term "sclerosis" is used chiefly. . .

DETD [0475] Multiple sclerosis is an autoimmune disease that in addition to chronic inflammation and demyelination, also results in gliosis within the central nervous system. There are several disease subtypes, including primary progressive multiple. . . subtypes may be distinguished from each other on the basis of the course of the disease, of the type of inflammation involved, and through the use of magnetic resonance imaging (MRI). It is also possible for the basic disease mechanism to change during the course of multiple sclerosis, with an inflammation-based process being replaced later by one which involves demyelination and axonal damage. See Weilbach and Gold, "Disease modifying treatments for. . .

DETD . . . compounds of Formula (1.0.0) also possess activity as immunosuppressive agents and are especially useful for treating autoimmune diseases in which inflammation is a component part of the autoimmune disease, or in which inflammation is part of the etiology of the autoimmune disease, or in which inflammation is otherwise involved with the autoimmune disease. Alternatively, the compounds of Formula (1.0.0) are anti-inflammatory agents useful in the treatment. . .

DETD . . . with the formation of pseudopolyps, i.e., edematous, inflamed islands of mucosa between areas of ulceration; and transmural colitis, which is inflammation of the full thickness of the bowel, rather than mucosal and submucosal disease, usually with the formation of noncaseating granulomas,. . .

DETD [0518] gout, and fever and pain associated with inflammation;

DETD [0523] uveitis of whatever type, etiology, or pathogenesis; or uveitis that is a member selected from the group consisting of inflammation of all or part of the uvea; anterior uveitis; iritis; cyclitis; iridocyclitis; granulomatous uveitis; nongranulomatous uveitis; phacoantigenic uveitis; posterior uveitis;. . .

DETD . . . anesthetics for relieving pain, irritation and itching, e.g., benzocaine, lidocaine, dibucaine, and pramoxine hydrochloride; topical analgesics for relieving pain and inflammation, e.g., methyl salicylate, camphor, menthol, and resorcinol; topical antiseptics for preventing infection, e.g., benzalkonium chloride and povidone-iodine; and vitamins and. . .

CLM What is claimed is:

. . . degenerative arthritis; infectious arthritis; Lyme arthritis; proliferative arthritis; psoriatic arthritis; and vertebral arthritis; gout, and fever and pain associated with inflammation; an eosinophil-related disorder of whatever type, etiology, or pathogenesis; or an eosinophil-related disorder that is a member selected from the. . . conjunctivitis; uveitis of whatever type, etiology, or pathogenesis; or uveitis that is a member selected from the group consisting of inflammation of all or part of the uvea; anterior uveitis; iritis; cyclitis; iridocyclitis; granulomatous uveitis; nongranulomatous uveitis; phacoantigenic uveitis; posterior uveitis;. . .

IT 50-24-8, Prednisolone 53-03-2, Prednisone 57-22-7, Vincristine 57-66-9, Probenecid 57-96-5, Sulfinpyrazone 58-55-9, Theophylline, biological studies 59-05-2, Methotrexate 59-42-7, Phenylephrine 64-86-8, Colchicine 76-25-5, Triamcinolone acetonide 90-82-4, Pseudoephedrine 101-40-6, Propylhexedrine 113-92-8, Chlorpheniramine 128-39-2D, 2,6-Di-tert-butylphenol, hydrazone derivs. 315-30-0, Allopurinol 317-34-0, Aminophylline 404-86-4, Capsaicin 446-86-6, Azathioprine 522-48-5, Tetrahydrozoline hydrochloride 550-99-2, Naphazoline hydrochloride 586-06-1, Metaproterenol 865-21-4, Vinblastine 1218-35-5, Xylometazoline hydrochloride 2315-02-8, Oxymetazoline hydrochloride 3198-07-0 3385-03-3, Flunisolide 3562-84-3, Benzbromarone 5534-09-8, Beclomethasone dipropionate 6339-87-3D, Thiophene-2-sulfonamide, derivs. 7440-57-5D, Gold, aurothio derivs. 7683-59-2, Isoproterenol 9004-08-4D, Cathepsin, derivs. 14838-15-4, Phenylpropanolamine 15826-37-6, Sodium cromoglycate 18559-94-9, Albuterol 22254-24-6, Ipratropium bromide 23031-25-6, Terbutaline 28797-61-7, Pirenzepine 30286-75-0, Oxitropium bromide 30392-40-6, Bitolterol 38677-81-5, Pirbuterol 51333-22-3, Budesonide 58581-89-8, Azelastine 59865-13-3, Cyclosporine 68844-77-9, Astemizole 73573-87-2, Formoterol 75706-12-6, Leflunomide 79794-75-5, Loratadine 80474-14-2, Fluticasone propionate 80880-90-6, Telenzepine 83799-24-0, Fexofenadine 83869-56-1, Granulocyte-macrophage colony-stimulating factor 83881-51-0, Cetirizine 83919-23-7, Mometasone furoate 89365-50-4, Salmeterol 93211-49-5, L-651392 96566-25-5, Ablukast 100643-71-8, Desloratadine 103177-37-3, Pranlukast 103475-41-8, Tepoxalin 106096-93-9, Basic fibroblast growth factor 107753-78-6, Zafirlukast 111406-87-2, Zileuton 118414-82-7, MK-886 120128-20-3, RG-12525 120443-16-5, Verlukast 126544-47-6, Ciclesonide 128253-31-6, BAY x 1005 128312-51-6 136310-93-5, Tiotropium bromide 140841-32-3 141579-54-6, Fenleuton 141579-87-5 143538-27-6, BAY x 7195 147030-01-1, MK-591 147398-01-4, CGS-25019c 147432-77-7, Ontazolast 151581-24-7, Iralukast 154355-76-7, ABT-761 158930-07-5, L-739010 158966-92-8, Montelukast 162011-90-7, Rofecoxib 162750-10-9, SB-210661 168154-07-2, L-746530 170277-31-3, Infliximab 171964-73-1, ZD-0892 174636-32-9, Talnetant 185243-69-0, Etanercept 202415-99-4 204974-93-6, BIIL 260 257892-34-5, D 4418 331731-18-1, D 2E7 346735-24-8, BIIL 284 350610-64-9, NKP-608C 446023-33-2, UT 77
(combination therapy with PDE4 inhibitors; preparation of carbamoyl-substituted pyridinyl aryl ether derivs. as inhibitors of PDE4 isoenzymes)

L23 ANSWER 5 OF 10 USPATFULL on STN
ACCESSION NUMBER: 2004:64384 USPATFULL <<LOGINID::20080303>>
TITLE: Nicotinamide biaryl derivatives useful as inhibitors of PDE4 isozymes
INVENTOR(S): Chambers, Robert J., Mystic, CT, UNITED STATES
Marfat, Anthony, Mystic, CT, UNITED STATES
Magee, Thomas V., Mystic, CT, UNITED STATES
PATENT ASSIGNEE(S): Pfizer Inc. (U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2004048903	A1	20040311

	US 6953810	B2	20051011
APPLICATION INFO.:	US 2003-613988	A1	20030702 (10)

RELATED APPLN. INFO.: Division of Ser. No. US 2002-62813, filed on 31 Jan 2002, GRANTED, Pat. No. US 6649633

	NUMBER	DATE
PRIORITY INFORMATION:	US 2001-265492P	20010131 (60)

DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: PFIZER INC., PATENT DEPARTMENT, MS8260-1611, EASTERN POINT ROAD, GROTON, CT, 06340
NUMBER OF CLAIMS: 18
EXEMPLARY CLAIM: 1
LINE COUNT: 7041
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

SUMM . . . for more selective inhibitors of PDEs that are able to suppress both immune cell functions in vitro and allergic pulmonary inflammation in vivo, while at the same time having improved side-effect profiles. Within the airways of patients suffering from asthma and. . .

SUMM [0008] Airflow obstruction and airway inflammation are features of asthma as well as COPD. While bronchial asthma is predominantly characterized by an eosinophilic inflammation, neutrophils appear to play a major role in the pathogenesis of COPD. Thus, PDEs that are involved in smooth muscle. . .

SUMM . . . hydrolases from their granules, and the generation of reactive oxygen species, neutrophils contribute to the tissue destruction associated with chronic inflammation, and are further implicated in the pathology of conditions such as emphysema.

SUMM . . . 400 mg; Pruniaux et al., "The novel phosphodiesterase inhibitor CI-1018 inhibits antigen-induced lung eosinophilia in sensitized brown-norway rats--comparison with rolipram," Inflammation S-04-6, 1999. CI-1018 has been demonstrated to have good oral bioavailability (57% in the rat) and good oral potency of. . .

SUMM [0202] gout, and fever and pain associated with inflammation;

SUMM [0207] uveitis of whatever type, etiology, or pathogenesis; or uveitis that is a member selected from the group consisting of inflammation of all or part of the uvea; anterior uveitis; iritis; cyclitis; iridocyclitis; granulomatous uveitis; nongranulomatous uveitis; phacoantigenic uveitis; posterior uveitis;. . .

SUMM . . . In particular, the compounds of Formula (1.0.0) are useful int the treatment of (1) inflammatory diseases and conditions comprising: joint inflammation, rheumatoid arthritis, rheumatoid spondylitis, osteoarthritis, inflammatory bowel disease, ulcerative colitis, chronic glomerulonephritis, dermatitis, and Crohn's disease; (2) respiratory diseases and. . .

SUMM . . . (1.0.0) is asthma, a chronic, increasingly common disorder encountered worldwide and characterized by intermittent reversible airway obstruction, airway hyper-responsiveness and inflammation . The cause of asthma has yet to be determined, but the most common pathological expression of asthma is inflammation of the airways, which may be significant even in the airways of patients with mild asthma. Based on bronchial biopsy. . .

SUMM [0393] Pulmonary Inflammation in Allergic Cynomolqus Monkeys

SUMM . . . use of primates, is that described in Turner et al.,

"Characterization of a primate model of asthma using anti-allergy/anti-asthma agents," Inflammation Research 45 239-245, 1996.

SUMM [0409] COPD is characterized by inflammation of the airways, as is the case with asthma, but the inflammatory cells that have been found in the bronchoalveolar. . .

SUMM . . . a productive cough; staphylococcus or streptococcal bronchitis which are caused by staphylococci or streptococci; and vesicular bronchitis in which the inflammation extends into the alveoli, which are sometimes visible under the pleura as whitish-yellow granulations like millet seeds.

SUMM . . . and T-lymphocytes. A variety of inflammatory mediators is also released by these cells, all of which may contribute to the inflammation exhibited in the late phase response.

SUMM . . . al "Effect of AWD 12-281, a new selective PDE-4 inhibitor, loteprednol and beclomethasone in models of allergic rhinitis and airway inflammation in brown norway-rats," Am. J. Respir. Crit. Care Med. A95, 1999. The compounds D-22888 and AWD-12,281 have already been described. . .

SUMM . . . rhinitis in terms of anatomical proximity as well as a shared etiology and pathogenesis in some cases. Sinusitis is the inflammation of a sinus and this condition may be purulent or nonpurulent, as well as acute or chronic. Depending upon the sinus where the inflammation is located, the condition is known as ethmoid, frontal, maxillary, or sphenoid sinusitis. The ethmoidal sinus is one type of. . .

SUMM [0429] Arthritis is defined as inflammation of the joints, and rheumatoid arthritis is a chronic systemic disease primarily of the joints, usually polyarticular, marked by inflammatory. . .

SUMM . . . Accordingly, the term "rheumatoid arthritis" includes acute arthritis, which is arthritis marked by pain, heat, redness, and swelling due to inflammation, infection, or trauma; acute gouty arthritis, which is acute arthritis associated with gout; chronic inflammatory arthritis, which is inflammation of the joints in chronic disorders such as rheumatoid arthritis; degenerative arthritis, which is osteoarthritis; infectious arthritis, which is arthritis. . . or parasites; Lyme arthritis, which is arthritis of the large joints associated with Lyme 20 disease; proliferative arthritis, which is inflammation of the joints with proliferation of the synovium, seen in rheumatoid arthritis; psoriatic arthritis, which is a syndrome in which psoriasis occurs in association with inflammatory arthritis; and vertebral arthritis, which is inflammation involving the intervertebral disks.

SUMM [0431] The three major pathological features of rheumatoid arthritis that are responsible for progressive joint destruction are inflammation, abnormal cellular and humoral responses, and synovial hyperplasia. The particular cellular pathology of rheumatoid arthritis includes the presence of T-cells. . . disease. Pro-inflammatory cytokines, e.g., IL-1, IL-4, IL-5, IL-6, IL-9, IL-13, and TNF-α, are the major contributors to joint tissue damage, inflammation, hyperplasia, pannus formation and bone resorption. See Firestein,. G. S. and Zvaifier, W. J., "How important are T-cells in chronic. . .

SUMM . . . of the compounds of Formula (1.0.0) to inhibit TNF-α release from stimulated monocytes can be correlated with animal models of inflammation in which anti-inflammatory effects can be

shown to correspond to suppression of TNF-α accumulation. One such animal model involves inhibition. . .

SUMM . . . are tophi or chalky deposits of sodium urate. Some therapeutic agents are useful in treating both gout and its attendant inflammation, e.g., phenylbutazone and colchicine; while other therapeutic agents possess only uricosuric properties, e.g., sulfinpyrazone and benzbromarone

SUMM . . . to the present invention such fever is either that manifested in pharyngoconjunctival fever or rheumatic fever, or that manifested during inflammation. A concomitant of inflammation is pain, especially that experienced in the joints and connective tissue of those suffering from rheumatoid arthritis and gout.

SUMM . . . PDE4 inhibitory compounds of Formula (1.0.0) provide beneficial results in the treatment of gout, and fever and pain associated with inflammation.

SUMM . . . PDE4 inhibitors and their utility in the treatment of rheumatoid arthritis. The activity of rolipram in animal models of acute inflammation such as the mouse adjuvant arthritis model, has been demonstrated in the art; Sekut et al, "Anti-inflammatory activity of phosphodiesterase (PDE) IV inhibitors in acute and chronic models of inflammation," Olin. Exp. Immunol. 100(1) 126-132, 1995. The ability of rolipram to reduce disease severity in the collagen II induced arthritis. . .

SUMM . . . the compound t.i.d. The compound was able to induce a positive trend towards clinical improvement associated with a reduction in C-reactive protein and IL-6 serum levels.
Chikanza et al, "The clinical effects of RP73401 phosphodiesterase Type 4 inhibitor in patients with rheumatoid. . .

SUMM . . . a central role in the induction of local IgE responses and the recruitment of eosinophils in this disease. The chronic inflammation seen in atopic dermatitis is considered to be the result of several interdependent factors, such as repeated or persistent allergen. . . vascular adhesion molecule-1 (VCAM-1), an adhesion molecule involved in the migration of mononuclear cells and eosinophils into sites of tissue inflammation. Further, IL-5 is a key mediator of eosinophil activation, which is a common feature of atopic disease.

SUMM . . . conjunctiva is a delicate membrane that lines the eyelids and covers the exposed surface of the sclera. Conjunctivitis is an inflammation of the conjunctiva that generally consists of conjunctival hyperemia associated with a discharge. The most common types of conjunctivitis, which. . . which is an acute conjunctivitis caused by bacteria or viruses, particularly gonococci, meningococci, pneumococci, and streptococci, and characterized by severe inflammation of the conjunctiva and copious discharge of pus; and vernal conjunctivitis which is a bilateral conjunctivitis of seasonal occurrence, of. . .

SUMM . . . is the vascular middle coat or tunic of the eye, comprising the iris, ciliary body, and choroid. Uveitis is an inflammation of all or part of the uvea and commonly involves the other tunics of the eye, i.e., the sclera and. . . the posterior portion, characterized by nodular collections of epithelioid cells and giant cells surrounded by lymphocytes; nongranulomatous uveitis which is inflammation of the anterior portion of the uveal tract, i.e., the iris and ciliary body; phacoantigenic uveitis which is one of. . .

SUMM . . . number of mediators via either topical or systemic

administration. For example, rolipram has been shown to inhibit croton oil-induced ear inflammation in the mouse at topical doses as low as 0.03 mg per ear. The selective PDE4 inhibitor Ro 20-1724 has. . .

SUMM [0460] A sclerosis is an induration, or hardening, and refers especially to hardening of a part from inflammation, and from increased formation of connective tissue and in diseases of the interstitial substance. The term "sclerosis" is used chiefly. . .

SUMM [0461] Multiple sclerosis is an autoimmune disease that in addition to chronic inflammation and demyelination, also results in gliosis within the central nervous system. There are several disease subtypes, including primary progressive multiple. . . subtypes may be distinguished from each other on the basis of the course of the disease, of the type of inflammation involved, and through the use of magnetic resonance imaging (MRI). It is also possible for the basic disease mechanism, to change during the course of multiple sclerosis, with an inflammation-based process being replaced later by one which involves demyelination and axonal damage. See Weilbach and Gold, "Disease modifying treatments for. . .

SUMM . . . compounds of Formula (1.0.0) also possess activity as immunosuppressive agents and are especially useful for treating autoimmune diseases in which inflammation is a component part of the autoimmune disease, or in which inflammation is part of the etiology of the autoimmune disease, or in which inflammation is otherwise involved with the autoimmune disease. Alternatively, the compounds of Formula (1.0.0) are anti-inflammatory agents useful in the treatment. . .

SUMM . . . with the formation of pseudopolyps, i.e., edematous, inflamed islands of mucosa between areas of ulceration; and transmural colitis, which is inflammation of the full thickness of the bowel, rather than mucosal and submucosal disease, usually with the formation of noncaseating granulomas,. . .

SUMM [0497] gout, and fever and pain associated with inflammation;

SUMM [0502] uveitis of whatever type, etiology, or pathogenesis; or uveitis that is a member selected from the group consisting of inflammation of all or part of the uvea; anterior uveitis; iritis; cyclitis; iridocyclitis; granulomatous uveitis; nongranulomatous uveitis; phacoantigenic uveitis; posterior uveitis;. . .

SUMM . . . anesthetics for relieving pain, irritation and itching, e.g., benzocaine, lidocaine, dibucaine, and pramoxine hydrochloride; topical analgesics for relieving pain and inflammation, e.g., methyl salicylate, camphor, menthol, and resorcinol; topical antiseptics for preventing infection, e.g., benzalkonium chloride and povidone-iodine; and vitamins and. . .

CLM What is claimed is:

. . . degenerative arthritis; infectious arthritis; Lyme arthritis; proliferative arthritis; psoriatic arthritis; and vertebral arthritis; gout, and fever and pain associated with inflammation; an eosinophil-related disorder of whatever type, etiology, or pathogenesis; or an eosinophil-related disorder that is a member selected from the. . . conjunctivitis; uveitis of whatever type, etiology, or pathogenesis; or uveitis that is a member selected from the group consisting of inflammation of all or part of the uvea; anterior uveitis; iritis; cyclitis; iridocyclitis; granulomatous uveitis; nongranulomatous uveitis; phacoantigenic uveitis; posterior uveitis;. . .

. . . disease, disorder, or condition is a member selected from the group

consisiting of (1) inflammatory diseases and conditions comprising: joint inflammation, rheumatoid arthritis, rheumatoid spondylitis, osteoarthritis, inflammatory bowel disease, ulcerative colitis, chronic glomerulonephritis, dermatitis, and Crohn's disease; (2) respiratory diseases and. . .

IT 57-22-7, Vincristine 57-66-9, Probenecid 57-96-5, Sulfinpyrazone 58-55-9, Theophylline, biological studies 59-05-2, Methotrexate 59-42-7, Phenylephrine 64-86-8, Colchicine 76-25-5, Triamcinolone acetonide 90-82-4, Pseudoephedrine 101-40-6, Propylhexedrine 113-92-8, Chlorpheniramine 315-30-0, Allopurinol 317-34-0, Aminophylline 446-86-6, Azathioprine 522-48-5, Tetrahydrozoline hydrochloride 550-99-2, Naphazoline hydrochloride 586-06-1, Orciprenaline 865-21-4, Vinblastine 1218-35-5, Xylometazoline hydrochloride 1397-89-3, Amphotericin B 1404-26-8, Polymyxin B 2315-02-8, Oxymetazoline hydrochloride 3198-07-0 3385-03-3, Flunisolide 3562-84-3, Benzbromarone 5534-09-8, Beclomethasone dipropionate 7440-57-5D, Gold, derivs. 7683-59-2, Isoprenaline 9004-08-4, Cathepsin 14838-15-4, Phenylpropanolamine 15826-37-6, Sodium cromoglycate 18559-94-9, Salbutamol 22254-24-6, Ipratropium bromide 22916-47-8, Miconazole 23031-25-6, Terbutaline 23593-75-1, Clotrimazole 27220-47-9, Econazole 30392-41-7, Bitolterol mesylate 38677-81-5, Pirbuterol 51333-22-3, Budesonide 58581-89-8, Azelastine 59865-13-3, Cyclosporine 65277-42-1, Ketoconazole 68844-77-9, Astemizole 73573-87-2, Formoterol 75706-12-6, Leflunomide 79794-75-5, Loratadine 80474-14-2, Fluticasone propionate 83799-24-0, Fexofenadine 83881-51-0, Cetirizine 83919-23-7, Mometasone furoate 86386-73-4, Fluconazole 89365-50-4, Salmeterol 93211-49-5, L-651392 96566-25-5, Ablukast 100643-71-8, Desloratadine 103177-37-3, Pranlukast 103475-41-8, Tepoxalin 107753-78-6, Zafirlukast 111406-87-2, Zileuton 118414-82-7, MK-886 120128-20-3, RG-12525 120443-16-5, Verlukast 126544-47-6, Ciclesonide 128253-31-6, BAY X 1005 140841-32-3, ZD 2138 141579-54-6, Fenleuton 143538-27-6, BAY x 7195 147030-01-1, MK-591 147398-01-4, CGS-25019c 147432-77-7, Ontazolast 151581-24-7, Iralukast 154355-76-7, ABT-761 158930-07-5, L-739010 158966-92-8, Montelukast 162011-90-7, Rofecoxib 162750-10-9, SB-210661 168154-07-2, L-746530 170277-31-3, Infliximab 185243-69-0, Etanercept 257892-34-5, D 4418 331731-18-1, D 2E7

(in combination with; preparation of biaryl nicotinamides as inhibitors of PDE4 isoenzymes)

L23 ANSWER 6 OF 10 USPATFULL on STN

ACCESSION NUMBER: 2003:265957 USPATFULL <<LOGINID::20080303>>

TITLE: Pyrrolyl- and imidazolyl-acid amide derivatives useful as inhibitors of PDE4 isozymes

INVENTOR(S): Marfat, Anthony, UNITED STATES
McKechney, Michael William, UNITED STATES

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2003186974	A1	20031002
	US 6869945	B2	20050322
APPLICATION INFO.:	US 2002-300950	A1	20021120 (10)

RELATED APPLN. INFO.: Division of Ser. No. US 2002-62145, filed on 31 Jan 2002, PENDING

	NUMBER	DATE
PRIORITY INFORMATION:	US 2001-265486P	20010131 (60)
DOCUMENT TYPE:	Utility	
FILE SEGMENT:	APPLICATION	
LEGAL REPRESENTATIVE:	PFIZER INC., PATENT DEPARTMENT, MS8260-1611, EASTERN POINT ROAD, GROTON, CT, 06340	
NUMBER OF CLAIMS:	10	
EXEMPLARY CLAIM:	1	
LINE COUNT:	7140	

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

SUMM . . . for more selective inhibitors of PDEs that are able to suppress both immune cell functions in vitro and allergic pulmonary inflammation in vivo, while at the same time having improved side-effect profiles. Within the airways of patients suffering from asthma and. . .

SUMM [0008] Airflow obstruction and airway inflammation are features of asthma as well as COPD. While bronchial asthma is predominantly characterized by an eosinophilic inflammation, neutrophils appear to play a major role in the pathogenesis of COPD. Thus, PDEs that are involved in smooth muscle. . .

SUMM . . . hydrolases from their granules, and the generation of reactive oxygen species, neutrophils contribute to the tissue destruction associated with chronic inflammation, and are further implicated in the pathology of conditions such as emphysema.

SUMM . . . 400 mg; Pruniaux et al., "The novel phosphodiesterase inhibitor CI-1018 inhibits antigen-induced lung eosinophilia in sensitized brown-norway rats--comparison with rolipram," Inflammation S-04-6, 1999. CI-1018 has been demonstrated to have good oral bioavailability (57% in the rat) and good oral potency of. . .

SUMM [0209] gout, and fever and pain associated with inflammation;

SUMM [0214] uveitis of whatever type, etiology, or pathogenesis; or uveitis that is a member selected from the group consisting of inflammation of all or part of the uvea; anterior uveitis; iritis; cyclitis; iridocyclitis; granulomatous uveitis; nongranulomatous uveitis; phacoantigenic uveitis; posterior uveitis;. . .

SUMM . . . In particular, the compounds of Formula (1.0.0) are useful int the treatment of (1) inflammatory diseases and conditions comprising: joint inflammation, rheumatoid arthritis, rheumatoid spondylitis, osteoarthritis, inflammatory bowel disease, ulcerative colitis, chronic glomerulonephritis, dermatitis, and Crohn's disease; (2) respiratory diseases and. . .

DETD . . . (1.0.0) is asthma, a chronic, increasingly common disorder encountered worldwide and characterized by intermittent reversible airway obstruction, airway hyper-responsiveness and inflammation . The cause of asthma has yet to be determined, but the most common pathological expression of asthma is inflammation of the airways, which may be significant even in the airways of patients with mild asthma. Based on bronchial biopsy. . .

DETD [0435] Pulmonary Inflammation in Allergic Cynomolqus Monkeys--The ability of the combinations of therapeutic agents of the present invention to inhibit Ascaris antigen induced. . .

DETD . . . use of primates, is that described in Turner et al., "Characterization of a primate model of asthma using anti-allergy/anti-asthma agents," Inflammation Research 45

239-245, 1996.

DETD [0450] COPD is characterized by inflammation of the airways, as is the case with asthma, but the inflammatory cells that have been found in the bronchoalveolar. . .

DETD . . . a productive cough; staphylococcus or streptococcal bronchitis which are caused by staphylococci or streptococci; and vesicular bronchitis in which the inflammation extends into the alveoli, which are sometimes visible under the pleura as whitish-yellow granulations like millet seeds.

DETD . . . and T-lymphocytes. A variety of inflammatory mediators is also released by these cells, all of which may contribute to the inflammation exhibited in the late phase response.

DETD . . . al "Effect of AWD 12-281, a new selective PDE-4 inhibitor, loteprednol and beclomethasone in models of allergic rhinitis and airway inflammation in brown norway-rats," Am. J. Respir. Crit. Care Med. A95, 1999. The compounds D-22888 and AWD-12,281 have already been described. . .

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DETD [0472] Arthritis is defined as inflammation of the joints, and rheumatoid arthritis is a chronic systemic disease primarily of the joints, usually polyarticular, marked by inflammatory. . .

DETD . . . Accordingly, the term "rheumatoid arthritis" includes acute arthritis, which is arthritis marked by pain, heat, redness, and swelling due to inflammation, infection, or trauma; acute gouty arthritis, which is acute arthritis associated with gout; chronic inflammatory arthritis, which is inflammation of the joints in chronic disorders such as rheumatoid arthritis; degenerative arthritis, which is osteoarthritis; infectious arthritis, which is arthritis. . . or parasites; Lyme arthritis, which is arthritis of the large joints associated with Lyme 20 disease; proliferative arthritis, which is inflammation of the joints with proliferation of the synovium, seen in rheumatoid arthritis; psoriatic arthritis, which is a syndrome in which psoriasis occurs in association with inflammatory arthritis; and vertebral arthritis, which is inflammation involving the intervertebral disks.

DETD [0474] The three major pathological features of rheumatoid arthritis that are responsible for progressive joint destruction are inflammation, abnormal cellular and humoral responses, and synovial hyperplasia. The particular cellular pathology of rheumatoid arthritis includes the presence of T-cells. . . disease. Pro-inflammatory cytokines, e.g., IL-1, IL-4, IL-5, IL-6, IL-9, IL-13, and TNF-α, are the major contributors to joint tissue damage, inflammation, hyperplasia, pannus formation and bone resorption. See Firestein,.G. S. and Zvaifier, W. J., "How important are T-cells in chronic rheumatoid. . .

DETD . . . of the compounds of Formula (1.0.0) to inhibit TNF-α release from stimulated monocytes can be correlated with animal models of inflammation in which anti-inflammatory effects can be shown to correspond to suppression of TNF-α accumulation. One such animal model involves inhibition. . .

DETD . . . are tophi or chalky deposits of sodium urate. Some therapeutic agents are useful in treating both gout and its attendant inflammation, e.g., phenylbutazone and colchicine; while other therapeutic agents possess only uricosuric properties, e.g., sulfinpyrazone and benzbromarone

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DETD . . . is the vascular middle coat or tunic of the eye, comprising the iris, ciliary body, and choroid. Uveitis is an inflammation of all or part of the uvea and commonly involves the other tunics of the eye, i.e., the sclera and. . . the posterior portion, characterized by nodular collections of epithelioid cells and giant cells surrounded by lymphocytes; nongranulomatous uveitis which is inflammation of the anterior portion of the uveal tract, i.e., the iris and ciliary body; phacoantigenic uveitis which is one of. . .

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low as 0.03 mg per ear. The selective PDE4 inhibitor Ro 20-1724 has. . .

DETD [0505] A sclerosis is an induration, or hardening, and refers especially to hardening of a part from inflammation, and from increased formation of connective tissue and in diseases of the interstitial substance. The term "sclerosis" is used chiefly. . .

DETD [0506] Multiple sclerosis is an autoimmune disease that in addition to chronic inflammation and demyelination, also results in gliosis within the central nervous system. There are several disease subtypes, including primary progressive multiple. . . subtypes may be distinguished from each other on the basis of the course of the disease, of the type of inflammation involved, and through the use of magnetic resonance imaging (MRI). It is also possible for the basic disease mechanism to change during the course of multiple sclerosis, with an inflammation-based process being replaced later by one which involves demyelination and axonal damage. See Weilbach and Gold, "Disease modifying treatments for. . .

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DETD . . . with the formation of pseudopolyps, i.e., edematous, inflamed islands of mucosa between areas of ulceration; and transmural colitis, which is inflammation of the full thickness of the bowel, rather than mucosal and submucosal disease, usually with the formation of noncaseating granulomas,. . .

DETD [0549] gout, and fever and pain associated with inflammation;

DETD [0554] uveitis of whatever type, etiology, or pathogenesis; or uveitis that is a member selected from the group consisting of inflammation of all or part of the uvea; anterior uveitis; iritis; cyclitis; iridocyclitis; granulomatous uveitis; nongranulomatous uveitis; phacoantigenic uveitis; posterior uveitis;. . .

DETD . . . anesthetics for relieving pain, irritation and itching, e.g., benzocaine, lidocaine, dibucaine, and pramoxine hydrochloride; topical analgesics for relieving pain and inflammation, e.g., methyl salicylate, camphor, menthol, and resorcinol; topical antiseptics for preventing infection, e.g., benzalkonium chloride and povidone-iodine; and vitamins and. . .

CLM What is claimed is:

. . . degenerative arthritis; infectious arthritis; Lyme arthritis; proliferative arthritis; psoriatic arthritis; and vertebral arthritis; gout, and fever and pain associated with inflammation; an eosinophil-related disorder of whatever type, etiology, or pathogenesis; or an eosinophil-related disorder that is a member selected from the. . . conjunctivitis; uveitis of whatever type, etiology, or pathogenesis; or uveitis that is a member selected from the group consisting of inflammation of all or part of the uvea; anterior uveitis; iritis; cyclitis; iridocyclitis; granulomatous uveitis; nongranulomatous uveitis; phacoantigenic uveitis; posterior uveitis;. . .

IT 57-22-7, Vincristine 57-66-9, Probenecid 57-96-5, Sulfinpyrazone 58-55-9, Theophylline, biological studies 59-05-2, Methotrexate 59-42-7, Phenylephrine 64-86-8, Colchicine 76-25-5, Triamcinolone

acetonide 90-82-4, Pseudoephedrine 91-22-5D, Quinoline, derivs. 101-40-6, Propylhexedrine 113-92-8, Chlorpheniramine 120-72-9D, Indole, derivs. 128-39-2D, 2,6-Di-tert-butylphenol, hydrazone derivs. 315-30-0, Allopurinol 317-34-0, Aminophylline 404-86-4, Capsaicin 446-86-6, Azathioprine 522-48-5, Tetrahydrozoline hydrochloride 550-99-2, Naphazoline hydrochloride 581-30-6, 3H-Phenothiazin-3-one 586-06-1, Orciprenaline 613-46-7D, 2-Cyanonaphthalene, pyridinyl derivs. 865-21-4, Vinblastine 1218-35-5, Xylometazoline hydrochloride 1436-43-7, 2-Cyanoquinoline 2315-02-8, Oxymetazoline hydrochloride 3198-07-0 3385-03-3, Flunisolide 3562-84-3, Benzbromarone 5534-09-8, Beclomethasone dipropionate 6339-87-3D, 2-Thiophenesulfonamide, derivs. 7440-57-5D, Gold, aurothio derivs. 7683-59-2, Isoprenaline 9004-08-4, Cathepsin 10102-43-9, Nitric oxide, biological studies 14838-15-4, Phenylpropanolamine 15826-37-6, Sodium cromoglycate 18559-94-9, Albuterol 22254-24-6, Ipratropium bromide 23031-25-6, Terbutaline 30392-41-7, Bitolterol mesylate 38677-81-5, Pirbuterol 51333-22-3, Budesonide 58581-89-8, Azelastine 59865-13-3, Cyclosporine 68844-77-9, Astemizole 73573-87-2, Formoterol 75706-12-6, Leflunomide 79554-19-1D, derivs. 79794-75-5, Loratadine 80474-14-2 , Fluticasone propionate 83799-24-0, Fexofenadine 83869-56-1, Granulocyte macrophage colony stimulating factor 83881-51-0, Cetirizine 83919-23-7, Mometasone furoate 89365-50-4, Salmeterol 93211-49-5, L-651392 96566-25-5, Ablukast 100643-71-8, Desloratadine 103177-37-3, Pranlukast 103475-41-8, Tepoxalin 106096-93-9, Basic fibroblast growth factor 107753-78-6, Zafirlukast 111406-87-2, Zileuton 118414-82-7, MK-886 120128-20-3, RG-12525 120443-16-5, Verlukast 126544-47-6, Ciclesonide 128253-31-6, BAY x 1005 128312-51-6 140841-32-3, ZD-2138 141579-54-6, Fenleuton 141579-87-5 143538-27-6, BAY x 7195 147030-01-1, MK-591 147398-01-4, CGS-25019c 147432-77-7, Ontazolast 151581-24-7, Iralukast 154355-76-7, ABT-761 158930-07-5, L-739010 158966-92-8, Montelukast 162011-90-7, Rofecoxib 162750-10-9, SB-210661 168154-07-2, L-746530 170277-31-3, Infliximab 185243-69-0, Etanercept 202415-99-4 204974-93-6, BIIL 260 257892-34-5, D 4418 331731-18-1, D 2E7 346735-24-8, BIIL 284
(combination therapy with PDE4 inhibitors; preparation of thiazolyl-, oxazolyl-, pyrrolyl-, and imidazolyl- acid amide derivs. as inhibitors of PDE4 isoenzymes)

L23 ANSWER 7 OF 10 USPATFULL on STN

ACCESSION NUMBER:	2003:188461 USPATFULL <<LOGINID::20080303>>
TITLE:	Oxazolyl-acid amide derivatives useful as inhibitors of PDE4 isozymes
INVENTOR(S):	Marfat, Anthony, UNITED STATES McKechney, Michael William, UNITED STATES

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2003130254	A1	20030710
	US 6894041	B2	20050517
APPLICATION INFO.:	US 2002-300959	A1	20021120 (10)
RELATED APPLN. INFO.:	Division of Ser. No. US 2002-62145, filed on 31 Jan 2002, PENDING		

	NUMBER	DATE

PRIORITY INFORMATION:	US 2001-265486P 20010131 (60)
DOCUMENT TYPE:	Utility
FILE SEGMENT:	APPLICATION
LEGAL REPRESENTATIVE:	PFIZER INC., PATENT DEPARTMENT, MS8260-1611, EASTERN POINT ROAD, GROTON, CT, 06340
NUMBER OF CLAIMS:	10
EXEMPLARY CLAIM:	1
LINE COUNT:	7168

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

SUMM . . . for more selective inhibitors of PDEs that are able to suppress both immune cell functions in vitro and allergic pulmonary inflammation in vivo, while at the same time having improved side-effect profiles. Within the airways of patients suffering from asthma and. . .

SUMM [0008] Airflow obstruction and airway inflammation are features of asthma as well as COPD. While bronchial asthma is predominantly characterized by an eosinophilic inflammation, neutrophils appear to play a major role in the pathogenesis of COPD. Thus, PDEs that are involved in smooth muscle. . .

SUMM . . . hydrolases from their granules, and the generation of reactive oxygen species, neutrophils contribute to the tissue destruction associated with chronic inflammation, and are further implicated in the pathology of conditions such as emphysema.

SUMM . . . 400 mg; Pruniaux et al., "The novel phosphodiesterase inhibitor Cl-1018 inhibits antigen-induced lung eosinophilia in sensitized brown-norway rats--comparison with rolipram," Inflammation S-04-6, 1999. Cl-1018 has been demonstrated to have good oral bioavailability (57% in the rat) and good oral potency of. . .

SUMM [0221] gout, and fever and pain associated with inflammation;

SUMM [0226] uveitis of whatever type, etiology, or pathogenesis; or uveitis that is a member selected from the group consisting of inflammation of all or part of the uvea; anterior uveitis; iritis; cyclitis; iridocyclitis; granulomatous uveitis; nongranulomatous uveitis; phacoantigenic uveitis; posterior uveitis;. . .

SUMM . . . In particular, the compounds of Formula (1.0.0) are useful int the treatment of (1) inflammatory diseases and conditions comprising: joint inflammation, rheumatoid arthritis, rheumatoid spondylitis, osteoarthritis, inflammatory bowel disease, ulcerative colitis, chronic glomerulonephritis, dermatitis, and Crohn's disease; (2) respiratory diseases and. . .

DETD . . . (1.0.0) is asthma, a chronic, increasingly common disorder encountered worldwide and characterized by intermittent reversible airway obstruction, airway hyper-responsiveness and inflammation . The cause of asthma has yet to be determined, but the most common pathological expression of asthma is inflammation of the airways, which may be significant even in the airways of patients with mild asthma. Based on bronchial biopsy. . .

DETD [0463] Pulmonary Inflammation in Allergic Cynomolqus Monkeys--The ability of the combinations of therapeutic agents of the present invention to inhibit Ascaris antigen induced. . .

DETD . . . use of primates, is that described in Turner et al., "Characterization of a primate model of asthma using anti-allergy/anti-asthma agents," Inflammation Research 45 239-245, 1996.

DETD [0478] COPD is characterized by inflammation of the airways,

as is the case with asthma, but the inflammatory cells that have been found in the bronchoalveolar. . .

DETD . . . a productive cough; staphylococcus or streptococcal bronchitis which are caused by staphylococci or streptococci; and vesicular bronchitis in which the inflammation extends into the alveoli, which are sometimes visible under the pleura as whitish-yellow granulations like millet seeds.

DETD . . . and T-lymphocytes. A variety of inflammatory mediators is also released by these cells, all of which may contribute to the inflammation exhibited in the late phase response.

DETD . . . al "Effect of AWD 12-281, a new selective PDE-4 inhibitor, loteprednol and beclomethasone in models of allergic rhinitis and airway inflammation in brown norway-rats," Am. J. Respir. Crit. Care Med. A95, 1999. The compounds D-22888 and AWD-12,281 have already been described. . .

DETD . . . rhinitis in terms of anatomical proximity as well as a shared etiology and pathogenesis in some cases. Sinusitis is the inflammation of a sinus and this condition may be purulent or nonpurulent, as well as acute or chronic. Depending upon the sinus where the inflammation is located, the condition is known as ethmoid, frontal, maxillary, or sphenoid sinusitis. The ethmoidal sinus is one type of. . .

DETD [0500] Arthritis is defined as inflammation of the joints, and rheumatoid arthritis is a chronic systemic disease primarily of the joints, usually polyarticular, marked by inflammatory. . .

DETD . . . Accordingly, the term "rheumatoid arthritis" includes acute arthritis, which is arthritis marked by pain, heat, redness, and swelling due to inflammation, infection, or trauma; acute gouty arthritis, which is acute arthritis associated with gout; chronic inflammatory arthritis, which is inflammation of the joints in chronic disorders such as rheumatoid arthritis; degenerative arthritis, which is osteoarthritis; infectious arthritis, which is arthritis. . . or parasites; Lyme arthritis, which is arthritis of the large joints associated with Lyme 20 disease; proliferative arthritis, which is inflammation of the joints with proliferation of the synovium, seen in rheumatoid arthritis; psoriatic arthritis, which is a syndrome in which psoriasis occurs in association with inflammatory arthritis; and vertebral arthritis, which is inflammation involving the intervertebral disks.

DETD [0502] The three major pathological features of rheumatoid arthritis that are responsible for progressive joint destruction are inflammation, abnormal cellular and humoral responses, and synovial hyperplasia. The particular cellular pathology of rheumatoid arthritis includes the presence of T-cells. . . disease. Pro-inflammatory cytokines, e.g., IL-1, IL-4, IL-5, IL-6, IL-9, IL-13, and TNF-α, are the major contributors to joint tissue damage, inflammation, hyperplasia, pannus formation and bone resorption. See Firestein,.G. S. and Zvaifier, W. J., "How important are T-cells in chronic rheumatoid. . .

DETD . . . of the compounds of Formula (1.0.0) to inhibit TNF-α release from stimulated monocytes can be correlated with animal models of inflammation in which anti-inflammatory effects can be shown to correspond to suppression of TNF-α accumulation. One such animal model involves inhibition. . .

DETD . . . are tophi or chalky deposits of sodium urate. Some therapeutic agents are useful in treating both gout and its attendant

inflammation, e.g., phenylbutazone and colchicine; while other therapeutic agents possess only uricosuric properties, e.g., sulfinpyrazone and benzbromarone

DETD . . . to the present invention such fever is either that manifested in pharyngoconjunctival fever or rheumatic fever, or that manifested during inflammation. A concomitant of inflammation is pain, especially that experienced in the joints and connective tissue of those suffering from rheumatoid arthritis and gout.

DETD . . . PDE4 inhibitory compounds of Formula (1.0.0) provide beneficial results in the treatment of gout, and fever and pain associated with inflammation.

DETD . . . PDE4 inhibitors and their utility in the treatment of rheumatoid arthritis. The activity of rolipram in animal models of acute inflammation such as the mouse adjuvant arthritis model, has been demonstrated in the art; Sekut et al, "Anti-inflammatory activity of phosphodiesterase (PDE) IV inhibitors in acute and chronic models of inflammation," Olin. Exp. Immunol. 100(1) 126-132, 1995. The ability of rolipram to reduce disease severity in the collagen II induced arthritis. . .

DETD . . . the compound t.i.d. The compound was able to induce a positive trend towards clinical improvement associated with a reduction in C-reactive protein and IL-6 serum levels.
Chikanza et al, "The clinical effects of RP73401 phosphodiesterase Type 4 inhibitor in patients with rheumatoid. . .

DETD . . . a central role in the induction of local IgE responses and the recruitment of eosinophils in this disease. The chronic inflammation seen in atopic dermatitis is considered to be the result of several interdependent factors, such as repeated or persistent allergen. . . vascular adhesion molecule-1 (VCAM-1), an adhesion molecule involved in the migration of mononuclear cells and eosinophils into sites of tissue inflammation. Further, IL-5 is a key mediator of eosinophil activation, which is a common feature of atopic disease.

DETD . . . conjunctiva is a delicate membrane that lines the eyelids and covers the exposed surface of the sclera. Conjunctivitis is an inflammation of the conjunctiva that generally consists of conjunctival hyperemia associated with a discharge. The most common types of conjunctivitis, which. . . which is an acute conjunctivitis caused by bacteria or viruses, particularly gonococci, meningococci, pneumococci, and streptococci, and characterized by severe inflammation of the conjunctiva and copious discharge of pus; and vernal conjunctivitis which is a bilateral conjunctivitis of seasonal occurrence, of. . .

DETD . . . is the vascular middle coat or tunic of the eye, comprising the iris, ciliary body, and choroid. Uveitis is an inflammation of all or part of the uvea and commonly involves the other tunics of the eye, i.e., the sclera and. . . the posterior portion, characterized by nodular collections of epithelioid cells and giant cells surrounded by lymphocytes; nongranulomatous uveitis which is inflammation of the anterior portion of the uveal tract, i.e., the iris and ciliary body; phacoantigenic uveitis which is one of. . .

DETD . . . number of mediators via either topical or systemic administration. For example, rolipram has been shown to inhibit croton oil-induced ear inflammation in the mouse at topical doses as low as 0.03 mg per ear. The selective PDE4 inhibitor Ro 20-1724 has. . .

DETD [0533] A sclerosis is an induration, or hardening, and refers especially to hardening of a part from inflammation, and from increased formation of connective tissue and in diseases of the interstitial substance. The term "sclerosis" is used chiefly. . .

DETD [0534] Multiple sclerosis is an autoimmune disease that in addition to chronic inflammation and demyelination, also results in gliosis within the central nervous system. There are several disease subtypes, including primary progressive multiple. . . subtypes may be distinguished from each other on the basis of the course of the disease, of the type of inflammation involved, and through the use of magnetic resonance imaging (MRI). It is also possible for the basic disease mechanism to change during the course of multiple sclerosis, with an inflammation-based process being replaced later by one which involves demyelination and axonal damage. See Weilbach and Gold, "Disease modifying treatments for. . .

DETD . . . compounds of Formula (1.0.0) also possess activity as immunosuppressive agents and are especially useful for treating autoimmune diseases in which inflammation is a component part of the autoimmune disease, or in which inflammation is part of the etiology of the autoimmune disease, or in which inflammation is otherwise involved with the autoimmune disease. Alternatively, the compounds of Formula (1.0.0) are anti-inflammatory agents useful in the treatment. . .

DETD . . . with the formation of pseudopolyps, i.e., edematous, inflamed islands of mucosa between areas of ulceration; and transmural colitis, which is inflammation of the full thickness of the bowel, rather than mucosal and submucosal disease, usually with the formation of noncaseating granulomas,. . .

DETD [0577] gout, and fever and pain associated with inflammation;

DETD [0582] uveitis of whatever type, etiology, or pathogenesis; or uveitis that is a member selected from the group consisting of inflammation of all or part of the uvea; anterior uveitis; iritis; cyclitis; iridocyclitis; granulomatous uveitis; nongranulomatous uveitis; phacoantigenic uveitis; posterior uveitis;. . .

DETD . . . anesthetics for relieving pain, irritation and itching, e.g., benzocaine, lidocaine, dibucaine, and pramoxine hydrochloride; topical analgesics for relieving pain and inflammation, e.g., methyl salicylate, camphor, menthol, and resorcinol; topical antiseptics for preventing infection, e.g., benzalkonium chloride and povidone-iodine; and vitamins and. . .

CLM What is claimed is:

. . . degenerative arthritis; infectious arthritis; Lyme arthritis; proliferative arthritis; psoriatic arthritis; and vertebral arthritis; gout, and fever and pain associated with inflammation; an eosinophil-related disorder of whatever type, etiology, or pathogenesis; or an eosinophil-related disorder that is a member selected from the. . . conjunctivitis; uveitis of whatever type, etiology, or pathogenesis; or uveitis that is a member selected from the group consisting of inflammation of all or part of the uvea; anterior uveitis; iritis; cyclitis; iridocyclitis; granulomatous uveitis; nongranulomatous uveitis; phacoantigenic uveitis; posterior uveitis;. . .

IT 57-22-7, Vincristine 57-66-9, Probenecid 57-96-5, Sulfinpyrazone 58-55-9, Theophylline, biological studies 59-05-2, Methotrexate 59-42-7, Phenylephrine 64-86-8, Colchicine 76-25-5, Triamcinolone acetonide 90-82-4, Pseudoephedrine 91-22-5D, Quinoline, derivs. 101-40-6, Propylhexedrine 113-92-8, Chlorpheniramine 120-72-9D,

Indole, derivs. 128-39-2D, 2,6-Di-tert-butylphenol, hydrazone derivs. 315-30-0, Allopurinol 317-34-0, Aminophylline 404-86-4, Capsaicin 446-86-6, Azathioprine 522-48-5, Tetrahydrozoline hydrochloride 550-99-2, Naphazoline hydrochloride 581-30-6, 3H-Phenothiazin-3-one 586-06-1, Orciprenaline 613-46-7D, 2-Cyanonaphthalene, pyridinyl derivs. 865-21-4, Vinblastine 1218-35-5, Xylometazoline hydrochloride 1436-43-7, 2-Cyanoquinoline 2315-02-8, Oxymetazoline hydrochloride 3198-07-0 3385-03-3, Flunisolide 3562-84-3, Benzbromarone 5534-09-8, Beclomethasone dipropionate 6339-87-3D, 2-Thiophenesulfonamide, derivs. 7440-57-5D, Gold, aurothio derivs. 7683-59-2, Isoprenaline 9004-08-4, Cathepsin 10102-43-9, Nitric oxide, biological studies 14838-15-4, Phenylpropanolamine 15826-37-6, Sodium cromoglycate 18559-94-9, Albuterol 22254-24-6, Ipratropium bromide 23031-25-6, Terbutaline 30392-41-7, Bitolterol mesylate 38677-81-5, Pirbuterol 51333-22-3, Budesonide 58581-89-8, Azelastine 59865-13-3, Cyclosporine 68844-77-9, Astemizole 73573-87-2, Formoterol 75706-12-6, Leflunomide 79554-19-1D, derivs. 79794-75-5, Loratadine 80474-14-2 , Fluticasone propionate 83799-24-0, Fexofenadine 83869-56-1, Granulocyte macrophage colony stimulating factor 83881-51-0, Cetirizine 83919-23-7, Mometasone furoate 89365-50-4, Salmeterol 93211-49-5, L-651392 96566-25-5, Ablukast 100643-71-8, Desloratadine 103177-37-3, Pranlukast 103475-41-8, Tepoxalin 106096-93-9, Basic fibroblast growth factor 107753-78-6, Zafirlukast 111406-87-2, Zileuton 118414-82-7, MK-886 120128-20-3, RG-12525 120443-16-5, Verlukast 126544-47-6, Ciclesonide 128253-31-6, BAY x 1005 128312-51-6 140841-32-3, ZD-2138 141579-54-6, Fenleuton 141579-87-5 143538-27-6, BAY x 7195 147030-01-1, MK-591 147398-01-4, CGS-25019c 147432-77-7, Ontazolast 151581-24-7, Iralukast 154355-76-7, ABT-761 158930-07-5, L-739010 158966-92-8, Montelukast 162011-90-7, Rofecoxib 162750-10-9, SB-210661 168154-07-2, L-746530 170277-31-3, Infliximab 185243-69-0, Etanercept 202415-99-4 204974-93-6, BIIL 260 257892-34-5, D 4418 331731-18-1, D 2E7 346735-24-8, BIIL 284
(combination therapy with PDE4 inhibitors; preparation of thiazolyl-, oxazolyl-, pyrrolyl-, and imidazolyl- acid amide derivs. as inhibitors of PDE4 isoenzymes)

L23 ANSWER 8 OF 10 USPATFULL on STN

ACCESSION NUMBER:	2003:38198 USPATFULL <<LOGINID::20080303>>
TITLE:	Ether derivatives useful as inhibitors of PDE4 isozymes
INVENTOR(S):	Marfat, Anthony, Mystic, CT, UNITED STATES Chambers, Robert J., Mystic, CT, UNITED STATES Magee, Thomas V., Mystic, CT, UNITED STATES
PATENT ASSIGNEE(S):	Pfizer Inc. (U.S. corporation)

	NUMBER	KIND	DATE	
PATENT INFORMATION:	US 2003027845	A1	20030206	
	US 6828333	B2	20041207	
APPLICATION INFO.:	US 2002-66503	A1	20020131	(10)

	NUMBER	DATE
PRIORITY INFORMATION:	US 2001-265304P	20010131 (60)
DOCUMENT TYPE:	Utility	

FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: PFIZER INC, 150 EAST 42ND STREET, 5TH FLOOR - STOP 49, NEW YORK, NY, 10017-5612
NUMBER OF CLAIMS: 30
EXEMPLARY CLAIM: 1
LINE COUNT: 8073
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

SUMM . . . for more selective inhibitors of PDEs that are able to suppress both immune cell functions in vitro and allergic pulmonary inflammation in vivo, while at the same time having improved side-effect profiles. Within the airways of patients suffering from asthma and. . .

SUMM [0008] Airflow obstruction and airway inflammation are features of asthma as well as COPD. While bronchial asthma is predominantly characterized by an eosinophilic inflammation, neutrophils appear to play a major role in the pathogenesis of COPD. Thus, PDEs that are involved in smooth muscle. . .

SUMM . . . hydrolases from their granules, and the generation of reactive oxygen species, neutrophils contribute to the tissue destruction associated with chronic inflammation, and are further implicated in the pathology of conditions such as emphysema.

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SUMM [0203] gout, and fever and pain associated with inflammation;

SUMM [0208] uveitis of whatever type, etiology, or pathogenesis; or uveitis that is a member selected from the group consisting of inflammation of all or part of the uvea; anterior uveitis; iritis; cyclitis; iridocyclitis; granulomatous uveitis; nongranulomatous uveitis; phacoantigenic uveitis; posterior uveitis;. . .

SUMM . . . In particular, the compounds of Formula (1.0.0) are useful in the treatment of (1) inflammatory diseases and conditions comprising: joint inflammation, rheumatoid arthritis, rheumatoid spondylitis, osteoarthritis, inflammatory bowel disease, ulcerative colitis, chronic glomerulonephritis, dermatitis, and Crohn's disease; (2) respiratory diseases and. . .

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SUMM [0404] Pulmonary Inflammation in Allergic Cynomolqus Monkeys

SUMM . . . use of primates, is that described in Turner et al., "Characterization of a primate model of asthma using anti-allergy/anti-asthma agents," Inflammation Research 45 239-245, 1996.

SUMM [0421] COPD is characterized by inflammation of the airways, as is the case with asthma, but the inflammatory cells that have been found in the bronchoalveolar. . .

SUMM . . . a productive cough; staphylococcus or streptococcal bronchitis which are caused by staphylococci or streptococci; and vesicular bronchitis in which the inflammation extends into the alveoli,

which are sometimes visible under the pleura as whitish-yellow granulations like millet seeds.

SUMM . . . and T-lymphocytes. A variety of inflammatory mediators is also released by these cells, all of which may contribute to the inflammation exhibited in the late phase response.

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SUMM . . . rhinitis in terms of anatomical proximity as well as a shared etiology and pathogenesis in some cases. Sinusitis is the inflammation of a sinus and this condition may be purulent or nonpurulent, as well as acute or chronic. Depending upon the sinus where the inflammation is located, the condition is known as ethmoid, frontal, maxillary, or sphenoid sinusitis. The ethmoidal sinus is one type of. . .

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SUMM . . . Accordingly, the term "rheumatoid arthritis" includes acute arthritis, which is arthritis marked by pain, heat, redness, and swelling due to inflammation, infection, or trauma; acute gouty arthritis, which is acute arthritis associated with gout; chronic inflammatory arthritis, which is inflammation of the joints in chronic disorders such as rheumatoid arthritis; degenerative arthritis, which is osteoarthritis; infectious arthritis, which is arthritis. . . or parasites; Lyme arthritis, which is arthritis of the large joints associated with Lyme 20 disease; proliferative arthritis, which is inflammation of the joints with proliferation of the synovium, seen in rheumatoid arthritis; psoriatic arthritis, which is a syndrome in which psoriasis occurs in association with inflammatory arthritis; and vertebral arthritis, which is inflammation involving the intervertebral disks.

SUMM [0446] The three major pathological features of rheumatoid arthritis that are responsible for progressive joint destruction are inflammation, abnormal cellular and humoral responses, and synovial hyperplasia. The particular cellular pathology of rheumatoid arthritis includes the presence of T-cells. . . disease. Pro-inflammatory cytokines, e.g., IL-1, IL-4, IL-5, IL-6, IL-9, IL-13, and TNF-α, are the major contributors to joint tissue damage, inflammation, hyperplasia, pannus formation and bone resorption. See Firestein, G. S. and Zvaifier, W. J., "How important are T-cells in chronic. . .

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SUMM . . . PDE4 inhibitors and their utility in the treatment of rheumatoid arthritis. The activity of rolipram in animal models of acute inflammation such as the mouse adjuvant arthritis model, has been demonstrated in the art; Sekut et al, "Anti-inflammatory activity of phosphodiesterase (PDE) IV inhibitors in acute and chronic models of inflammation," Olin. Exp. Immunol 100(1) 126-132, 1995. The ability of rolipram to reduce disease severity in the collagen II induced arthritis. . .

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SUMM . . . a central role in the induction of local IgE responses and the recruitment of eosinophils in this disease. The chronic inflammation seen in atopic dermatitis is considered to be the result of several interdependent factors, such as repeated or persistent allergen. . . vascular adhesion molecule-1 (VCAM-1), an adhesion molecule involved in the migration of mononuclear cells and eosinophils into sites of tissue inflammation. Further, IL-5 is a key mediator of eosinophil activation, which is a common feature of atopic disease.

SUMM . . . conjunctiva is a delicate membrane that lines the eyelids and covers the exposed surface of the sclera. Conjunctivitis is an inflammation of the conjunctiva that generally consists of conjunctival hyperemia associated with a discharge. The most common types of conjunctivitis, which. . . which is an acute conjunctivitis caused by bacteria or viruses, particularly gonococci, meningococci, pneumococci, and streptococci, and characterized by severe inflammation of the conjunctiva and copious discharge of pus; and vernal conjunctivitis which is a bilateral conjunctivitis of seasonal occurrence, of. . .

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SUMM [0478] A sclerosis is an induration, or hardening, and refers especially to hardening of a part from inflammation, and from increased formation of connective tissue and in diseases of the interstitial substance. The term "sclerosis" is used chiefly. . .

SUMM [0479] Multiple sclerosis is an autoimmune disease that in addition to

chronic inflammation and demyelination, also results in gliosis within the central nervous system. There are several disease subtypes, including primary progressive multiple. . . subtypes may be distinguished from each other on the basis of the course of the disease, of the type of inflammation involved, and through the use of magnetic resonance imaging (MRI). It is also possible for the basic disease mechanism to change during the course of multiple sclerosis, with an inflammation-based process being replaced later by one which involves demyelination and axonal damage. See Weilbach and Gold, "Disease modifying treatments for. . .

SUMM . . . compounds of Formula (1.0.0) also possess activity as immunosuppressive agents and are especially useful for treating autoimmune diseases in which inflammation is a component part of the autoimmune disease, or in which inflammation is part of the etiology of the autoimmune disease, or in which inflammation is otherwise involved with the autoimmune disease. Alternatively, the compounds of Formula (1.0.0) are anti-inflammatory agents useful in the treatment. . .

SUMM . . . with the formation of pseudopolyps, i.e., edematous, inflamed islands of mucosa between areas of ulceration; and transmural colitis, which is inflammation of the full thickness of the bowel, rather than mucosal and submucosal disease, usually with the formation of noncaseating granulomas,. . .

SUMM [0522] gout, and fever and pain associated with inflammation;

SUMM [0527] uveitis of whatever type, etiology, or pathogenesis; or uveitis that is a member selected from the group consisting of inflammation of all or part of the uvea; anterior uveitis; iritis; cyclitis; iridocyclitis; granulomatous uveitis; nongranulomatous uveitis; phacoantigenic uveitis; posterior uveitis;. . .

SUMM . . . anesthetics for relieving pain, irritation and itching, e.g., benzocaine, lidocaine, dibucaine, and pramoxine hydrochloride; topical analgesics for relieving pain and inflammation, e.g., methyl salicylate, camphor, menthol, and resorcinol; topical antiseptics for preventing infection, e.g., benzalkonium chloride and povidone-iodine; and vitamins and. . .

CLM What is claimed is:

. . . degenerative arthritis; infectious arthritis; Lyme arthritis; proliferative arthritis; psoriatic arthritis; and vertebral arthritis; gout, and fever and pain associated with inflammation; an eosinophil-related disorder of whatever type, etiology, or pathogenesis; or an eosinophil-related disorder that is a member selected from the. . . conjunctivitis; uveitis of whatever type, etiology, or pathogenesis; or uveitis that is a member selected from the group consisting of inflammation of all or part of the uvea; anterior uveitis; iritis; cyclitis; iridocyclitis; granulomatous uveitis; nongranulomatous uveitis; phacoantigenic uveitis; posterior uveitis;. . .

. . . disease, disorder, or condition is a member selected from the group consisting of (1) inflammatory diseases and conditions comprising: joint inflammation, rheumatoid arthritis, rheumatoid spondylitis, osteoarthritis, inflammatory bowel disease, ulcerative colitis, chronic glomerulonephritis, dermatitis, and Crohn's disease; (2) respiratory diseases and. . .

IT 50-24-8, Prednisolone 53-03-2, Prednisone 57-22-7, Vincristine 57-66-9, Probenecid 57-96-5, Sulfinpyrazone 58-55-9, Theophylline, biological studies 59-05-2, Methotrexate 59-42-7, Phenylephrine 64-86-8, Colchicine 76-25-5, Triamcinolone acetonide 90-82-4,

Pseudoephedrine 101-40-6, Propylhexedrine 113-92-8, Chlorpheniramine 128-39-2D, 2,6-Di-tert-butylphenol, hydrazone derivs. 315-30-0, Allopurinol 317-34-0, Aminophylline 404-86-4, Capsaicin 446-86-6, Azathioprine 522-48-5, Tetrahydrozoline hydrochloride 550-99-2, Naphazoline hydrochloride 586-06-1, Metaproterenol 865-21-4, Vinblastine 1218-35-5, Xylometazoline hydrochloride 2315-02-8, Oxymetazoline hydrochloride 3198-07-0 3385-03-3, Flunisolide 3562-84-3, Benzbromarone 5534-09-8, Beclomethasone dipropionate 6339-87-3D, Thiophene-2-sulfonamide, derivs. 7440-57-5D, Gold, aurothio derivs. 7683-59-2, Isoproterenol 9004-08-4D, Cathepsin, derivs. 14838-15-4, Phenylpropanolamine 15826-37-6, Sodium cromoglycate 18559-94-9, Albuterol 22254-24-6, Ipratropium bromide 23031-25-6, Terbutaline 28797-61-7, Pirenzepine 30286-75-0, Oxitropium bromide 30392-40-6, Bitolterol 38677-81-5, Pirbuterol 51333-22-3, Budesonide 58581-89-8, Azelastine 59865-13-3, Cyclosporine 68844-77-9, Astemizole 73573-87-2, Formoterol 75706-12-6, Leflunomide 79794-75-5, Loratadine 80474-14-2, Fluticasone propionate 80880-90-6, Telenzepine 83799-24-0, Fexofenadine 83869-56-1, Granulocyte-macrophage colony-stimulating factor 83881-51-0, Cetirizine 83919-23-7, Mometasone furoate 89365-50-4, Salmeterol 93211-49-5, L-651392 96566-25-5, Ablukast 100643-71-8, Desloratadine 103177-37-3, Pranlukast 103475-41-8, Tepoxalin 106096-93-9, Basic fibroblast growth factor 107753-78-6, Zafirlukast 111406-87-2, Zileuton 118414-82-7, MK-886 120128-20-3, RG-12525 120443-16-5, Verlukast 126544-47-6, Ciclesonide 128253-31-6, BAY x 1005 128312-51-6 136310-93-5, Tiotropium bromide 140841-32-3 141579-54-6, Fenleuton 141579-87-5 143538-27-6, BAY x 7195 147030-01-1, MK-591 147398-01-4, CGS-25019c 147432-77-7, Ontazolast 151581-24-7, Iralukast 154355-76-7, ABT-761 158930-07-5, L-739010 158966-92-8, Montelukast 162011-90-7, Rofecoxib 162750-10-9, SB-210661 168154-07-2, L-746530 170277-31-3, Infliximab 171964-73-1, ZD-0892 174636-32-9, Talnetant 185243-69-0, Etanercept 202415-99-4 204974-93-6, BIIL 260 257892-34-5, D 4418 331731-18-1, D 2E7 346735-24-8, BIIL 284 350610-64-9, NKP-608C 446023-33-2, UT 77

(combination therapy with PDE4 inhibitors; preparation of carbamoyl-substituted pyridinyl aryl ether derivs. as inhibitors of PDE4 isoenzymes)

L23 ANSWER 9 OF 10 USPATFULL on STN

ACCESSION NUMBER: 2002:338241 USPATFULL <<LOGINID::20080303>>

TITLE: Nicotinamide biaryl derivatives useful as inhibitors of PDE4 isozymes

INVENTOR(S): Chambers, Robert J., Mystic, CT, UNITED STATES
Marfat, Anthony, Mystic, CT, UNITED STATES
Magee, Thomas V., Mystic, CT, UNITED STATES

PATENT ASSIGNEE(S): Pfizer Inc. (U.S. corporation)

	NUMBER	KIND	DATE	
PATENT INFORMATION:	US 2002193612	A1	20021219	
	US 6649633	B2	20031118	
APPLICATION INFO.:	US 2002-62813	A1	20020131	(10)

	NUMBER	DATE

PRIORITY INFORMATION:	US 2001-265492P 20010131 (60)
DOCUMENT TYPE:	Utility
FILE SEGMENT:	APPLICATION
LEGAL REPRESENTATIVE:	PFIZER INC, 150 EAST 42ND STREET, 5TH FLOOR - STOP 49, NEW YORK, NY, 10017-5612
NUMBER OF CLAIMS:	18
EXEMPLARY CLAIM:	1
LINE COUNT:	7001

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

SUMM . . . for more selective inhibitors of PDEs that are able to suppress both immune cell functions in vitro and allergic pulmonary inflammation in vivo, while at the same time having improved side-effect profiles. Within the airways of patients suffering from asthma and. . .

SUMM [0008] Airflow obstruction and airway inflammation are features of asthma as well as COPD. While bronchial asthma is predominantly characterized by an eosinophilic inflammation, neutrophils appear to play a major role in the pathogenesis of COPD. Thus, PDEs that are involved in smooth muscle. . .

SUMM . . . hydrolases from their granules, and the generation of reactive oxygen species, neutrophils contribute to the tissue destruction associated with chronic inflammation, and are further implicated in the pathology of conditions such as emphysema.

SUMM . . . 400 mg; Pruniaux et al., "The novel phosphodiesterase inhibitor Cl-1018 inhibits antigen-induced lung eosinophilia in sensitized brown-norway rats--comparison with rolipram," Inflammation S-04-6, 1999. Cl-1018 has been demonstrated to have good oral bioavailability (57% in the rat) and good oral potency of. . .

SUMM [0192] gout, and fever and pain associated with inflammation;

SUMM [0197] uveitis of whatever type, etiology, or pathogenesis; or uveitis that is a member selected from the group consisting of inflammation of all or part of the uvea; anterior uveitis; iritis; cyclitis; iridocyclitis; granulomatous uveitis; nongranulomatous uveitis; phacoantigenic uveitis; posterior uveitis;. . .

SUMM . . . In particular, the compounds of Formula (1.0.0) are useful int the treatment of (1) inflammatory diseases and conditions comprising: joint inflammation, rheumatoid arthritis, rheumatoid spondylitis, osteoarthritis, inflammatory bowel disease, ulcerative colitis, chronic glomerulonephritis, dermatitis, and Crohn's disease; (2) respiratory diseases and. . .

SUMM . . . (1.0.0) is asthma, a chronic, increasingly common disorder encountered worldwide and characterized by intermittent reversible airway obstruction, airway hyper-responsiveness and inflammation . The cause of asthma has yet to be determined, but the most common pathological expression of asthma is inflammation of the airways, which may be significant even in the airways of patients with mild asthma. Based on bronchial biopsy. . .

SUMM [0410] Pulmonary Inflammation in Allergic Cynomolgus Monkeys--The ability of the combinations of therapeutic agents of the present invention to inhibit Ascaris antigen induced. . .

SUMM . . . use of primates, is that described in Turner et al., "Characterization of a primate model of asthma using anti-allergy/anti-asthma agents," Inflammation Research 45 239-245, 1996.

SUMM [0425] COPD is characterized by inflammation of the airways,

as is the case with asthma, but the inflammatory cells that have been found in the bronchoalveolar. . .

SUMM . . . a productive cough; staphylococcus or streptococcal bronchitis which are caused by staphylococci or streptococci; and vesicular bronchitis in which the inflammation extends into the alveoli, which are sometimes visible under the pleura as whitish-yellow granulations like millet seeds.

SUMM . . . and T-lymphocytes. A variety of inflammatory mediators is also released by these cells, all of which may contribute to the inflammation exhibited in the late phase response.

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SUMM . . . rhinitis in terms of anatomical proximity as well as a shared etiology and pathogenesis in some cases. Sinusitis is the inflammation of a sinus and this condition may be purulent or nonpurulent, as well as acute or chronic. Depending upon the sinus where the inflammation is located, the condition is known as ethmoid, frontal, maxillary, or sphenoid sinusitis. The ethmoidal sinus is one type of. . .

SUMM [0447] Arthritis is defined as inflammation of the joints, and rheumatoid arthritis is a chronic systemic disease primarily of the joints, usually polyarticular, marked by inflammatory. . .

SUMM . . . Accordingly, the term "rheumatoid arthritis" includes acute arthritis, which is arthritis marked by pain, heat, redness, and swelling due to inflammation, infection, or trauma; acute gouty arthritis, which is acute arthritis associated with gout; chronic inflammatory arthritis, which is inflammation of the joints in chronic disorders such as rheumatoid arthritis; degenerative arthritis, which is osteoarthritis; infectious arthritis, which is arthritis. . . or parasites; Lyme arthritis, which is arthritis of the large joints associated with Lyme 20 disease; proliferative arthritis, which is inflammation of the joints with proliferation of the synovium, seen in rheumatoid arthritis; psoriatic arthritis, which is a syndrome in which psoriasis occurs in association with inflammatory arthritis; and vertebral arthritis, which is inflammation involving the intervertebral disks.

SUMM [0449] The three major pathological features of rheumatoid arthritis that are responsible for progressive joint destruction are inflammation, abnormal cellular and humoral responses, and synovial hyperplasia. The particular cellular pathology of rheumatoid arthritis includes the presence of T-cells. . . disease. Pro-inflammatory cytokines, e.g., IL-1, IL-4, IL-5, IL-6, IL-9, IL-13, and TNF-α, are the major contributors to joint tissue damage, inflammation, hyperplasia, pannus formation and bone resorption. See Firestein, G. S. and Zvaifier, W. J., "How important are T-cells in chronic. . .

SUMM . . . of the compounds of Formula (1.0.0) to inhibit TNF-α release from stimulated monocytes can be correlated with animal models of inflammation in which anti-inflammatory effects can be shown to correspond to suppression of TNF-α accumulation. One such animal model involves inhibition. . .

SUMM . . . are tophi or chalky deposits of sodium urate. Some therapeutic agents are useful in treating both gout and its attendant

inflammation, e.g., phenylbutazone and colchicine; while other therapeutic agents possess only uricosuric properties, e.g., sulfinpyrazone and benzbromarone.

SUMM . . . to the present invention such fever is either that manifested in pharyngoconjunctival fever or rheumatic fever, or that manifested during inflammation. A concomitant of inflammation is pain, especially that experienced in the joints and connective tissue of those suffering from rheumatoid arthritis and gout.

SUMM . . . PDE4 inhibitory compounds of Formula (1.0.0) provide beneficial results in the treatment of gout, and fever and pain associated with inflammation.

SUMM . . . PDE4 inhibitors and their utility in the treatment of rheumatoid arthritis. The activity of rolipram in animal models of acute inflammation such as the mouse adjuvant arthritis model, has been demonstrated in the art; Sekut et al, "Anti-inflammatory activity of phosphodiesterase (PDE) IV inhibitors in acute and chronic models of inflammation," Olin. Exp. Immunol. 100(1) 126-132, 1995. The ability of rolipram to reduce disease severity in the collagen 11 induced arthritis. . .

SUMM . . . the compound t.i.d. The compound was able to induce a positive trend towards clinical improvement associated with a reduction in C-reactive protein and IL-6 serum levels.
Chikanza et al, "The clinical effects of RP73401 phosphodiesterase Type 4 inhibitor in patients with rheumatoid. . .

SUMM . . . a central role in the induction of local IgE responses and the recruitment of eosinophils in this disease. The chronic inflammation seen in atopic dermatitis is considered to be the result of several interdependent factors, such as repeated or persistent allergen. . . vascular adhesion molecule-1 (VCAM-1), an adhesion molecule involved in the migration of mononuclear cells and eosinophils into sites of tissue inflammation. Further, IL-5 is a key mediator of eosinophil activation, which is a common feature of atopic disease.

SUMM . . . conjunctiva is a delicate membrane that lines the eyelids and covers the exposed surface of the sclera. Conjunctivitis is an inflammation of the conjunctiva that generally consists of conjunctival hyperemia associated with a discharge. The most common types of conjunctivitis, which. . . which is an acute conjunctivitis caused by bacteria or viruses, particularly gonococci, meningococci, pneumococci, and streptococci, and characterized by severe inflammation of the conjunctiva and copious discharge of pus; and vernal conjunctivitis which is a bilateral conjunctivitis of seasonal occurrence, of. . .

SUMM . . . is the vascular middle coat or tunic of the eye, comprising the iris, ciliary body, and choroid. Uveitis is an inflammation of all or part of the uvea and commonly involves the other tunics of the eye, i.e., the sclera and. . . the posterior portion, characterized by nodular collections of epithelioid cells and giant cells surrounded by lymphocytes; nongranulomatous uveitis which is inflammation of the anterior portion of the uveal tract, i.e., the iris and ciliary body; phacoantigenic uveitis which is one of. . .

SUMM . . . number of mediators via either topical or systemic administration. For example, rolipram has been shown to inhibit croton oil-induced ear inflammation in the mouse at topical doses as low as 0.03 mg per ear. The selective PDE4 inhibitor Ro 20-1724 has. . .

SUMM [0480] A sclerosis is an induration, or hardening, and refers especially to hardening of a part from inflammation, and from increased formation of connective tissue and in diseases of the interstitial substance. The term "sclerosis" is used chiefly. . .

SUMM [0481] Multiple sclerosis is an autoimmune disease that in addition to chronic inflammation and demyelination, also results in gliosis within the central nervous system. There are several disease subtypes, including primary progressive multiple. . . subtypes may be distinguished from each other on the basis of the course of the disease, of the type of inflammation involved, and through the use of magnetic resonance imaging (MRI). It is also possible for the basic disease mechanism to change during the course of multiple sclerosis, with an inflammation-based process being replaced later by one which involves demyelination and axonal damage. See Weilbach and Gold, "Disease modifying treatments for. . .

SUMM . . . compounds of Formula (1.0.0) also possess activity as immunosuppressive agents and are especially useful for treating autoimmune diseases in which inflammation is a component part of the autoimmune disease, or in which inflammation is part of the etiology of the autoimmune disease, or in which inflammation is otherwise involved with the autoimmune disease. Alternatively, the compounds of Formula (1.0.0) are anti-inflammatory agents useful in the treatment. . .

SUMM . . . with the formation of pseudopolyps, i.e., edematous, inflamed islands of mucosa between areas of ulceration; and transmural colitis, which is inflammation of the full thickness of the bowel, rather than mucosal and submucosal disease, usually with the formation of noncaseating granulomas,. . .

SUMM [0524] gout, and fever and pain associated with inflammation;

SUMM [0529] uveitis of whatever type, etiology, or pathogenesis; or uveitis that is a member selected from the group consisting of inflammation of all or part of the uvea; anterior uveitis; iritis; cyclitis; iridocyclitis; granulomatous uveitis; nongranulomatous uveitis; phacoantigenic uveitis; posterior uveitis;. . .

SUMM . . . anesthetics for relieving pain, irritation and itching, e.g., benzocaine, lidocaine, dibucaine, and pramoxine hydrochloride; topical analgesics for relieving pain and inflammation, e.g., methyl salicylate, camphor, menthol, and resorcinol; topical antiseptics for preventing infection, e.g., benzalkonium chloride and povidone-iodine; and vitamins and. . .

CLM What is claimed is:

. . . degenerative arthritis; infectious arthritis; Lyme arthritis; proliferative arthritis; psoriatic arthritis; and vertebral arthritis; gout, and fever and pain associated with inflammation; an eosinophil-related disorder of whatever type, etiology, or pathogenesis; or an eosinophil-related disorder that is a member selected from the. . . conjunctivitis; uveitis of whatever type, etiology, or pathogenesis; or uveitis that is a member selected from the group consisting of inflammation of all or part of the uvea; anterior uveitis; iritis; cyclitis; iridocyclitis; granulomatous uveitis; nongranulomatous uveitis; phacoantigenic uveitis; posterior uveitis;. . .

. . . disease, disorder, or condition is a member selected from the group consisiting of (1) inflammatory diseases and conditions comprising: joint inflammation, rheumatoid arthritis, rheumatoid spondylitis, osteoarthritis, inflammatory bowel disease, ulcerative colitis, chronic glomerulonephritis, dermatitis, and Crohn's disease;

(2) respiratory diseases and. . .
IT 57-22-7, Vincristine 57-66-9, Probenecid 57-96-5, Sulfinpyrazone 58-55-9, Theophylline, biological studies 59-05-2, Methotrexate 59-42-7, Phenylephrine 64-86-8, Colchicine 76-25-5, Triamcinolone acetonide 90-82-4, Pseudoephedrine 101-40-6, Propylhexedrine 132-22-9, Chlorpheniramine 315-30-0, Allopurinol 317-34-0, Aminophylline 446-86-6, Azathioprine 522-48-5, Tetrahydrozoline hydrochloride 550-99-2, Naphazoline hydrochloride 586-06-1, Orciprenaline 865-21-4, Vinblastine 1218-35-5, Xylometazoline hydrochloride 1397-89-3, Amphotericin B 1404-26-8, Polymyxin B 2315-02-8, Oxymetazoline hydrochloride 3198-07-0 3385-03-3, Flunisolide 3562-84-3, Benzbromarone 5534-09-8, Beclomethasone dipropionate 7440-57-5D, Gold, derivs. 7683-59-2, Isoprenaline 9004-08-4, Cathepsin 14838-15-4, Phenylpropanolamine 15826-37-6, Sodium cromoglycate 18559-94-9, Salbutamol 22254-24-6, Ipratropium bromide 22916-47-8, Miconazole 23031-25-6, Terbutaline 23593-75-1, Clotrimazole 27220-47-9, Econazole 30392-41-7, Bitolterol mesylate 38677-81-5, Pirbuterol 51333-22-3, Budesonide 58581-89-8, Azelastine 59865-13-3, Cyclosporine 65277-42-1, Ketoconazole 68844-77-9, Astemizole 73573-87-2, Formoterol 75706-12-6, Leflunomide 79794-75-5, Loratadine 80474-14-2, Fluticasone propionate 83799-24-0, Fexofenadine 83881-51-0, Cetirizine 83919-23-7, Mometasone furoate 86386-73-4, Fluconazole 89365-50-4, Salmeterol 93211-49-5, L-651392 96566-25-5, Ablukast 100643-71-8, Desloratadine 103177-37-3, Pranlukast 103475-41-8, Tepoxalin 107753-78-6, Zafirlukast 111406-87-2, Zileuton 118414-82-7, MK-886 120128-20-3, RG-12525 120443-16-5, Verlukast 126544-47-6, Ciclesonide 128253-31-6, BAY X 1005 140841-32-3, ZD 2138 141579-54-6, Fenleuton 143538-27-6, BAY x 7195 147030-01-1, MK-591 147398-01-4, CGS-25019c 147432-77-7, Ontazolast 151581-24-7, Iralukast 154355-76-7, ABT-761 158930-07-5, L-739010 158966-92-8, Montelukast 162011-90-7, Rofecoxib 162750-10-9, SB-210661 168154-07-2, L-746530 170277-31-3, Infliximab 185243-69-0, Etanercept 257892-34-5, D 4418 331731-18-1, D 2E7
(in combination with; preparation of biaryl nicotinamides as inhibitors of PDE4 isoenzymes)

L23 ANSWER 10 OF 10 USPATFULL on STN
ACCESSION NUMBER: 2002:228358 USPATFULL <<LOGINID::20080303>>
TITLE: Thiazolyl-, oxazolyl-, pyrrolyl-, and imidazolyl-acid amide derivatives useful as inhibitors of PDE4 isozymes
INVENTOR(S): Marfat, Anthony, Mystic, CT, UNITED STATES
McKechney, Michael William, Fairport, NY, UNITED STATES
PATENT ASSIGNEE(S): Pfizer Inc. (U.S. corporation)

	NUMBER	KIND	DATE	
PATENT INFORMATION:	US 2002123520	A1	20020905	
	US 6559168	B2	20030506	
APPLICATION INFO.:	US 2002-62145	A1	20020131	(10)

	NUMBER	DATE
PRIORITY INFORMATION:	US 2001-265486P	20010131 (60)

DOCUMENT TYPE: Utility

FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: PFIZER INC, 150 EAST 42ND STREET, 5TH FLOOR - STOP 49, NEW YORK, NY, 10017-5612
NUMBER OF CLAIMS: 10
EXEMPLARY CLAIM: 1
LINE COUNT: 6963
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

SUMM . . . for more selective inhibitors of PDEs that are able to suppress both immune cell functions in vitro and allergic pulmonary inflammation in vivo, while at the same time having improved side-effect profiles. Within the airways of patients suffering from asthma and. . .

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SUMM [0208] gout, and fever and pain associated with inflammation;

SUMM [0213] uveitis of whatever type, etiology, or pathogenesis; or uveitis that is a member selected from the group consisting of inflammation of all or part of the uvea; anterior uveitis; iritis; cyclitis; iridocyclitis; granulomatous uveitis; nongranulomatous uveitis; phacoantigenic uveitis; posterior uveitis;. . .

SUMM . . . In particular, the compounds of Formula (1.0.0) are useful int the treatment of (1) inflammatory diseases and conditions comprising: joint inflammation, rheumatoid arthritis, rheumatoid spondylitis, osteoarthritis, inflammatory bowel disease, ulcerative colitis, chronic glomerulonephritis, dermatitis, and Crohn's disease; (2) respiratory diseases and. . .

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SUMM [0435] Pulmonary Inflammation in Allergic Cynomolgus Monkeys

SUMM . . . use of primates, is that described in Turner et al., "Characterization of a primate model of asthma using anti-allergy/anti-asthma agents," Inflammation Research 45 239-245, 1996.

SUMM [0452] COPD is characterized by inflammation of the airways, as is the case with asthma, but the inflammatory cells that have been found in the bronchoalveolar. . .

SUMM . . . a productive cough; staphylococcus or streptococcal bronchitis which are caused by staphylococci or streptococci; and vesicular bronchitis in which the inflammation extends into the alveoli,

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SUMM [0477] The three major pathological features of rheumatoid arthritis that are responsible for progressive joint destruction are inflammation, abnormal cellular and humoral responses, and synovial hyperplasia. The particular cellular pathology of rheumatoid arthritis includes the presence of T-cells. . . disease. Pro-inflammatory cytokines, e.g., IL-1, IL-4, IL-5, IL-6, IL-9, IL-13, and TNF-α, are the major contributors to joint tissue damage, inflammation, hyperplasia, pannus formation and bone resorption. See Firestein,.G. S. and Zvaifier, W. J., "How important are T-cells in chronic rheumatoid. . .

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SUMM [0510] A sclerosis is an induration, or hardening, and refers especially to hardening of a part from inflammation, and from increased formation of connective tissue and in diseases of the interstitial substance. The term "sclerosis" is used chiefly. . .

SUMM [0511] Multiple sclerosis is an autoimmune disease that in addition to

chronic inflammation and demyelination, also results in gliosis within the central nervous system. There are several disease subtypes, including primary progressive multiple. . . subtypes may be distinguished from each other on the basis of the course of the disease, of the type of inflammation involved, and through the use of magnetic resonance imaging (MRI). It is also possible for the basic disease mechanism to change during the course of multiple sclerosis, with an inflammation-based process being replaced later by one which involves demyelination and axonal damage. See Weilbach and Gold, "Disease modifying treatments for. . .

SUMM . . . compounds of Formula (1.0.0) also possess activity as immunosuppressive agents and are especially useful for treating autoimmune diseases in which inflammation is a component part of the autoimmune disease, or in which inflammation is part of the etiology of the autoimmune disease, or in which inflammation is otherwise involved with the autoimmune disease. Alternatively, the compounds of Formula (1.0.0) are anti-inflammatory agents useful in the treatment. . .

SUMM . . . with the formation of pseudopolyps, i.e., edematous, inflamed islands of mucosa between areas of ulceration; and transmural colitis, which is inflammation of the full thickness of the bowel, rather than mucosal and submucosal disease, usually with the formation of noncaseating granulomas,. . .

SUMM [0554] gout, and fever and pain associated with inflammation;

SUMM [0559] uveitis of whatever type, etiology, or pathogenesis; or uveitis that is a member selected from the group consisting of inflammation of all or part of the uvea; anterior uveitis; iritis; cyclitis; iridocyclitis; granulomatous uveitis; nongranulomatous uveitis; phacoantigenic uveitis; posterior uveitis;. . .

SUMM . . . anesthetics for relieving pain, irritation and itching, e.g., benzocaine, lidocaine, dibucaine, and pramoxine hydrochloride; topical analgesics for relieving pain and inflammation, e.g., methyl salicylate, camphor, menthol, and resorcinol; topical antiseptics for preventing infection, e.g., benzalkonium chloride and povidone-iodine; and vitamins and. . .

CLM What is claimed is:

. . . degenerative arthritis; infectious arthritis; Lyme arthritis; proliferative arthritis; psoriatic arthritis; and vertebral arthritis; gout, and fever and pain associated with inflammation; an eosinophil-related disorder of whatever type, etiology, or pathogenesis; or an eosinophil-related disorder that is a member selected from the. . . conjunctivitis; uveitis of whatever type, etiology, or pathogenesis; or uveitis that is a member selected from the group consisting of inflammation of all or part of the uvea; anterior uveitis; iritis; cyclitis; iridocyclitis; granulomatous uveitis; nongranulomatous uveitis; phacoantigenic uveitis; posterior uveitis;. . .

IT 57-22-7, Vincristine 57-66-9, Probenecid 57-96-5, Sulfinpyrazone 58-55-9, Theophylline, biological studies 59-05-2, Methotrexate 59-42-7, Phenylephrine 64-86-8, Colchicine 76-25-5, Triamcinolone acetonide 90-82-4, Pseudoephedrine 91-22-5D, Quinoline, derivs. 101-40-6, Propylhexedrine 120-72-9D, Indole, derivs. 128-39-2D, 2,6-Di-tert-butylphenol, hydrazone derivs. 132-22-9, Chlorpheniramine 315-30-0, Allopurinol 317-34-0, Aminophylline 404-86-4, Capsaicin 446-86-6, Azathioprine 522-48-5, Tetrahydrozoline hydrochloride 550-99-2, Naphazoline hydrochloride 581-30-6, 3H-Phenothiazin-3-one 586-06-1, Orciprenaline 613-46-7D, 2-Cyanonaphthalene, pyridinyl

derivs. 865-21-4, Vinblastine 1218-35-5, Xylometazoline hydrochloride 1436-43-7, 2-Cyanoquinoline 2315-02-8, Oxymetazoline hydrochloride 3198-07-0 3385-03-3, Flunisolide 3562-84-3, Benzbromarone 5534-09-8, Beclomethasone dipropionate 6339-87-3D, 2-Thiophenesulfonamide, derivs. 7440-57-5D, Gold, aurothio derivs. 7683-59-2, Isoprenaline 9004-08-4, Cathepsin 10102-43-9, Nitric oxide, biological studies 14838-15-4, Phenylpropanolamine 15826-37-6, Sodium cromoglycate 18559-94-9, Albuterol 22254-24-6, Ipratropium bromide 23031-25-6, Terbutaline 30392-41-7, Bitolterol mesylate 38677-81-5, Pirbuterol 51333-22-3, Budesonide 58581-89-8, Azelastine 59865-13-3, Cyclosporine 68844-77-9, Astemizole 73573-87-2, Formoterol 75706-12-6, Leflunomide 79554-19-1D, derivs. 79794-75-5, Loratadine 80474-14-2 , Fluticasone propionate 83799-24-0, Fexofenadine 83869-56-1, Granulocyte macrophage colony stimulating factor 83881-51-0, Cetirizine 83919-23-7, Mometasone furoate 89365-50-4, Salmeterol 93211-49-5, L-651392 96566-25-5, Ablukast 100643-71-8, Desloratadine 103177-37-3, Pranlukast 103475-41-8, Tepoxalin 106096-93-9, Basic fibroblast growth factor 107753-78-6, Zafirlukast 111406-87-2, Zileuton 118414-82-7, MK-886 120128-20-3, RG-12525 120443-16-5, Verlukast 126544-47-6, Ciclesonide 128253-31-6, BAY x 1005 128312-51-6 140841-32-3, ZD-2138 141579-54-6, Fenleuton 141579-87-5 143538-27-6, BAY x 7195 147030-01-1, MK-591 147398-01-4, CGS-25019c 147432-77-7, Ontazolast 151581-24-7, Iralukast 154355-76-7, ABT-761 158930-07-5, L-739010 158966-92-8, Montelukast 162011-90-7, Rofecoxib 162750-10-9, SB-210661 168154-07-2, L-746530 170277-31-3, Infliximab 185243-69-0, Etanercept 202415-99-4 204974-93-6, BIIL 260 257892-34-5, D 4418 331731-18-1, D 2E7 346735-24-8, BIIL 284
(combination therapy with PDE4 inhibitors; preparation of thiazolyl-, oxazolyl-, pyrrolyl-, and imidazolyl- acid amide derivs. as inhibitors of PDE4 isoenzymes)

=> FIL STNGUIDE

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	133.56	235.69

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION
CA SUBSCRIBER PRICE	-1.60	-1.60

FILE 'STNGUIDE' ENTERED AT 09:29:17 ON 03 MAR 2008

FILE CONTAINS CURRENT INFORMATION.
LAST RELOADED: Feb 29, 2008 (20080229/UP).

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